LIMB SALVAGE SURGERY WITH CUSTOM MADE PROSTHESIS FOR PROXIMAL TIBIAL OSTEOSARCOMAS

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CERTIFICATE

I hereby certify that this dissertation on **"*Limb savlage surgery with custom made prosthesis for proximal tibial osteosarcomas*"** is a bonafide work done by **DR. VINAY V GADIGI,** in the department of Surgical Oncology, College of Oncological Sciences, Cancer Institute (WIA), Chennai, under my guidance and supervision, to my satisfaction.

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AIMS OF THE STUDY

1. TO STUDY THE SURVIVAL OUTCOMES OF THE PATIENTS UNDERGOING LIMB SALVAGE SURGERY IN PROXIMAL TIBIAL TUMOURS WITH CUSTOM MADE MEGAPROSTHESIS.

2. TO COMPARE THE QUALITY OF LIFE ASSESSMENT BETWEEN GROUPS UNDERGOING EXTENSOR MECHANISM RECONSTRUCTION WITH OR WITHOUT A PROLENE MESH.

3. TO STUDY THE EARLY AND LATE COMPLICATIONS.

4. TO STUDY THE PROSTHESIS SURVIVAL TIME AND THE FACTORS AFFECTING PROSTHESIS SURVIVAL.

INTRODUCTION

"Walking is man's best* medicine"** ***- Hippocrates

Bony sarcomas arising from the proximal end of the tibia constitute the second most common site of occurrenceafter the distal end of the femur. However this area is a difficult site to perform a safe limb sparing resection in which function is preserved due to anatomical constraints and also surgical technique. Historically amputation had been the treatment for bony sarcomas. The use of effective chemotherapeutic regimen, modern imaging technology and advances in surgical techniques has broadened the horizon and scope of limb salvage surgery in this site. The primary difficulty in doing a limb salvage surgery for sarcoma of the proximal tibia is due to the local anatomy. A difficult surgical approach, intimate relationship to the neurovascular structures, inadequate soft tissue coverage are few of the challenges surgeons face during procedures at this site. Another important factor is the need to reconstruct the extensor mechanism of the knee joint. Many surgical techniques and reconstruction mechanisms have been described for the tumours at this site and have provided satisfactory survival and functional outcomes.

REVIEW OF LITERATURE

HISTORY OF BONE SARCOMAS

Osteosarcoma as a disease was recognised since ancient times. An English surgeon named John Abernathy coined the term "sarcoma" in 1804 which was derived from Greek roots and means "fleshy excrescence."[1] Alexis Boyer a French surgeon (personal surgeon to Napoleon) recognised that sarcomas arising in the bone are a distinct entity from other bony lesion and is credited with using the term osteosarcomas for the first time in 1805.[1]

The gross pathological appearance of this tumour was accurately described by Guillaume Dupuytren in 1847. He the described the appearance as the following:

"Osteosarcoma, which is a true cancerous degeneration of bone, manifests itself in the form of a white or reddish mass, lardaceous and firm at an early stage of the disease; but presenting at a later period, points of softening, cerebriform matter, extravasating blood, and white or straw coloured fluid of a viscid consistence in its interior."[1]

As there was limited experience to guide the surgeons of that time a Registry of Bone Sarcoma was created in 1921 under the auspices of the American College of Surgeons, by Ernest Amory Codman (along with James Ewing and Joseph Bloodgood).[2]

Great advances were made in the field of pathology of bone tumours in the mid-1900s. Henry Jaffe and Louis Lichtenstein published textbooks on bone pathology that established many of the important pathological criteria which are used to diagnose the commonly seen bone tumours.

Dr Norman Jaffe and few others popularised the use of chemotherapeutic drugs for osteosarcomas in the 1970s and early 1980s.[3] Most commonly Adriamycin and methotrexate were used. At MSKCC Rosen found out that these chemotherapeutic drugs useful both

preoperatively as well as postoperatively while studying the patients who were awaiting the custom made prosthesis for their surgery.[4]

William F. Enneking is an eminent name in the field of orthopaedic oncology. He introduced the a surgical staging system for bone sarcomas and trained many orthopaedic oncology fellows, several research papers have been published by him and actively conducted continuing medical education course on bone tumours.

The staging system described by Enneking et al is based on GTM: grade(G), location(T), lymph node involvement and metastasis (M). The staging system is as follows:

Stage IA (G1 T1 M0): Low grade intra-compartmental lesion, without metastasis.

Stage IB (G1 T2 M0): Low grade extra-compartmental lesion, without metastasis.

Stage IIA (G2 T1 M0): High grade intra-compartmental lesion, without metastasis.

Stage IIB (G2 T2 M0): High grade extra-compartmental lesion, without metastasis.

Stage IIIA (G1 or G2 T1 M1): Any grade intra-compartmental lesion with regional nodal or distant metastasis.

Stage IIIB (G1 or G2 T2 M1): Any grade extra-compartmental lesion with metastasis.

HISTORY OF LIMB SALVAGE SURGERY AND CUSTOM MADE PROSTHESIS

Amputation was the traditional treatment for osteosarcomsEiselberg in 1897 and Klapp in 1900 are probably the first people to perform limb salvage surgery and used bone grafts to reconstruct the defects. Lexter introduced the concept of using allografts in tumour surgeries. The concept of resection arthrodesis was introduced by Phemister for lesions above the knee and this technique was further refined by Merle D' Aubigne and Dejouany.

Till the 1960s the limb salvage surgery for bone tumours was restricted to benign and lower grade tumours. The development of newer reconstructive techniques including internal fixation led to the cautious use of limb salvage surgeries in high grade sarcomas.[6]

In the 1970s the improvements in imaging techniques (CT scans) and use of effective chemotherapeutic agents led to great advances in the limb salvage surgeries. Musculoskeletal Tumour Society (MSTS) was formed in this decade and met for the first time in 1979.[6]

In the 1980s there were tremendous advances in orthopaedic oncology. Surgical staging system was developed, surgical margins were defined and International Society on Limb Salvage (ISOLS) was formed in 1981. In the ISOLS meet in 1981 they reported a local recurrence rate of 18% and reconstructive failures in 15% and the second symposium held in 1983 in Vienna reported a local recurrence of 11% and reconstructive failures in 10%. The third meet held at Orlando reported a further declinein local recurrence (7%) and reconstructive failures (5%).[6]

PROXIMAL TIBIAL OSTEOSARCOMAS

The most common site of primary bone tumours is distal end of the femur and the proximal end of the tibia is the second most common site. 12% to 15% of osteosarcomas, 11% of Ewing's sarcoma and 6% of chondrosarcomas are located at the proximal end of the tibia.[7,8]The treatment for the proximal tibial tumours was routine amputation before the 1970s. Cades in 1955 followed a regimen of local radiotherapy and followed by amputation only if there was no evidence of distant spread within 6 months, however the outlook remained poor.[9]

Over the past 25 years the concept of limb salvage surgery has grown dramatically. Adriamycin- and methotrexate based chemotherapy which was introduced in the 1970s at Memorial–Sloan Kettering, New York University, and the Children's Hospital of Philadelphia made a huge impact in the prognosis and management of patients with bone sarcomas. Pioneering work by surgeons such as Ralph Marcove, Kenneth Francis, andHugh Watts led to the development of the techniques of limb salvage surgery.

Nowadays 90–95% of patients with extremitysarcomas who are being treated at centres specializingin musculoskeletal oncology are undergoing limb salvage surgery successfully. Advances in several fields have brought about this dramatic change. The following advances are the important ones among them.

1. Tumour biology and natural history are better understood.
2. There exists an effective induction chemotherapy with which even borderline cases can be salvaged.
3. Advancements in surgical techniques have brought about better functional outcomes. Even limbs in which the vessels have been involved can be salvaged with vascular grafts.
4. Better appreciation of biomechanics of the musculoskeletal system has led to better designing of the prosthesis and better outcomes functionally.

5. Novel materials are being used in the manufacturing of prosthesis due to advances in material engineering.

6. Prosthesis has been developed for virtually every site in the extremity which has been affected by bony tumours.[10]

However when considering a limb salvage surgery instead of an amputation certain factors have to be kept in mind

1) There should not be an increased risk to the patient's life because of the procedure.

2) Functional result should be better.

3) Complication rate must be acceptably low.

4) Patient and attenders must be fully informed about the procedure, the complications and the rehabilitation process.[9]

Several technical issues have to be addressed for the successful outcome of a limb salvage surgery.

a. Key neurovascular structures must be identified and preserved.
b. Oncological safe margins must be obtained, and preservation of a limb must never take priority over thesurvival of the patient. Meticulous surgical technique is necessary for achieving a safe margin
c. Reconstruction of the axial skeleton must be done with appropriate prosthesis
d. Restoration of good soft-tissue cover isnecessary for good prosthesis function and life.[10]

Patient selection for limb salvage surgeries

The introduction of effective chemotherapeutic agents for osteosarcoma has expanded the scope of limb salvage surgery. But the increased survival rates have now placed greater

importance on the functional outcome and the prosthesis survival. Today reconstruction has to take into account the functional, cosmetic and also the psychological needs of the patient.[10]

The most important factors that decide about decision to perform a limb salvage surgery successfully are location of the tumour and the involvement of neurovascular structures.

Picci et al. listed 6 anatomical sites where providing sufficient margins for resection is a problem.[11]

1. Popliteal space.
2. Joint structures.
3. Medullary canal.
4. Soft tissue involvement.
5. Venous thrombi.
6. Sites of periosteal reaction.

However with the use of preoperative chemotherapy many patients who are borderline candidates for limb salvage surgery upfront may ultimately become candidates for limb salvage surgery. The patient should always be re-evaluated after the completionof the chemotherapy and only then the final decision to proceed or not to proceed with the limb salvage surgery must be taken.

The proximal tibial bony sarcomas are a challenging group of tumours in the perspective of limb salvage. Surgical approach to these tumours is difficult, anatomical constraints and inadequate soft tissue cover make providing adequate margins and reconstruction at this site challenging. Providing a good functional outcome with reconstruction of the extensor mechanism is an important aspect of the reconstruction and rehabilitation of this subgroup of patient.

ANATOMICAL CONSIDERATIONS IN THE PROXIMAL TIBIAL SARCOMAS[12]

A. Popliteal artery trifurcation.

Thepopliteal trifurcation is actually a combination of two successive bifurcations. First the anterior tibial arises from the popliteal artery at the lower border of the popliteus.The popliteal artery continues as the tibioperoneal trunk and then bifurcates into peroneal artery and the posterior tibial artery. It may be necessary to ligate the anterior tibial artery to provide adequate soft tissue clearance. The popliteus muscle on the posterior surface of the tibia provides a barrier to the posterior soft tissue extension from the tibia and protects the popliteal artery and its branches.[12]

B. Tibiofibular joint.

Tumours of the proximal tibia have a high incidence of involvement of the tissues of the proximal tibiofibular joint. An en-bloc resection of this joint is usually necessary to provide adequate margin, especially for high grade sarcomas.[12]

C. Knee joint.

The knee joint is not usually directly involved by the tumours of the proximal tibia. This can occur if there has been a fracture or contamination due to a ill performed biopsy procedure. Hemarthrosis suggests intra-articular extension of the disease. MRI of the knee joint provides the most accurate assessment of the knee joint involvement. If knee joint involvement is suspected an extra-articular resection has to be planned.[12]

D. Extensor mechanism.

The reconstruction of the extensor mechanism by reattaching the patellar tendon is a challenging aspect of limb salvage surgery of the proximal tibia. Reconstruction of this

mechanism is necessary for a good function of the lower limb. Various mechanisms of reconstruction of the extensor mechanisms have been tried over the years and these will be described later.[12]

E. Subcutaneous location and less soft tissue coverage.

The medial aspect of the entire length of the tibia occupies the subcutaneous location. This leaves the reconstructed prosthesis in a subcutaneous location and is an important source of infection and prosthesis failure. The use of the medial gastrocnemius muscle has led to provision of adequate soft tissue cover for reconstruction and reduced the incidence of infection, flap necrosis, and secondary infection.[12]The musculotendinous insertion of the medial gastrocnemius was divided and it was rotated to cover the prosthesis and the reconstructed extensor mechanism and sutured to the underlying patellar tendon and the quadriceps muscle.[17]

Various options exist for the reconstruction of these tumours

1. Resection arthrodesis.

Prior to the 1970s this was the main method of reconstruction. It had the advantages of providing good stability, and a durable reconstruction. But as there was no movement at the reconstructed limb as the knee joint was resected and as the result the quality of life was poor. Nowadays due to adequate preservation of soft tissue as a result of effective chemotherapy and use of medial gastrocnemius for soft tissue cover this method is rarely followed.[10]

Fig 1. Intraoperative photograph of resection arthrodesis using dual fibular reconstruction with an intramedullary rod fixation following resection of the distal femur, a technique popularized by Dr William F. Enneking during 1970s.[10]

2. Van Nesrotationoplasty.

This procedure was first described by Borggreve in 1930, but later Van Nes popularized it. Here the lower limb is rotated by 180^0 by knee arthrodesis after resection of the tumour, such that at skeletal maturity the ankle joint of the short limb should be at the level of the contralateral limb knee joint. The foot acts like the residual tibia in a below knee amputation. The functional outcome of Van Nesrotationoplasty is significanty better and also needs less energy expenditure compared to the use of an above knee prosthesis.

Some disadvantages with this procedure are the failure to achieve sufficient rotation during the procedure, subsequent derotation due to continued growth of the skeleton and the unattractive appearance of the leg in which a reversed foot is used. However there are several reports of good patient acceptance and functional outcomes and also acceptable cosmetic acceptance by the patients, prosthetists and surgeons.[13,14,15,16]

3. Allograft reconstruction.

In the 1970s the allograft reconstruction was introduced as a biological solution to the problem of restoring a segmental defect of the skeleton. There have been significant advances in the techniques of fixation of these prostheses and also in the methods of processing the graft so as to preserve the articular cartilage and to lessen the contamination. In spite of these advances the use of allografts is not very popular due to the high rates of complication and prosthesis failure and also due to the stringent means needed to store these grafts. These grafts are procured according to the established guidelines and stored in a fresh frozen state at -80^0C. Even though the allografts are immunogenic the immune response is reduced by the non-vascularity of the graft and also due to the freezing which reduces the antigenicity. The osteoarticular allografts have certain advantages compared to the metallic endoprosthesis. They provide articular surface for the adjacent bone and obviate the need for resection of the articular surface and the growth plate. They also provide ligaments for joint reconstruction and including cruciate ligaments and sites for host tendon reconstruction and provides better functional outcome than the metallic endoprosthesis. However these advantages are offset by significant complications.Early complications are infection,non-union and joint instability, and late complications are instability and allograft fracture.The overall complication rate is more than 50%,which includes an infection rate of 30%. As a reason this is being done at few centres nowadays. This a good option in young patients who are expected to grow and develop substantial limb length discrepancies.

Fig 2. Allograft reconstruction of a proximal tibial tumour.[18]

4. Metallic endoprosthetic reconstruction.

Reconstruction of the proximal tibial tumours by endoprosthesis has been a highly successful procedure. They are either custom made prosthesis or else modular prosthesis. They are made of different alloys, but currently titanium alloy is the preferred one. The custom made prosthesis is relatively less expensive than the modular ones. The modular ones have the advantage of deciding on table for reconstruction depending upon the amount of bone resected. Whereas the custom made prosthesis are prefabricated and is subject to the variations in the tumour size and extent changes during therapy. Bone cement that is polymethlymethacrylate is usually used to fix this prosthesis. A press-fit porous stem can also be used instead of using bone cement. In a retrospective study of 1001 custom made prosthesis (which included 493 distal

femoral, 263 proximal femoral and 245 proximal tibial prostheses) aseptic loosening was shown to be the principal mode of failure of the implants.[19] Use of cemented stem allows instant fixation which will allow early rehabilitation and mobilization.

Improvements in the prosthesis design have also led to the improvements in prosthesis survival. In a study by Myers comparing the fixed hinge prosthesis and the rotating hinge prosthesis they found risk of revision for any reason in the fixed-hinge group was 32% at five years, 61% at ten years and 75% at 15 and 20 years, and in the rotating-hinge group 12% at five years, 25% at 10 years and 30% at 15 years. The cemented, rotating hinge design currently offers the best chance of long-term survival of the prosthesis.[20]

Expandable prosthesis is a novel innovation which is very helpful in for replacement in skeletally immature patients. In most of the commonly used expanding prosthesis a surgical procedure is usually required for the subsequent expansions. A novel type of expanding prosthesis called the Stanmore expandable prosthesis (Stanmore Implants, Stanmore Middlesex, United Kingdom) uses a noninvasive technique for the prosthesis expansion. When the patient with the expandable prosthesis is placed at the centre of a rotating electromagnetic field the poles of the magnet within expandable segment of the prosthesis are captured, causing it to rotate. The external field rotates slowly at a fixed speed causing the implant to expand at a rate of 0.23mm per minute (1mm every 4min).

5. Allograft prosthetic composite.

This prosthesis is a transitional step in between the allografts and the metallic endoprosthesis. This was introduced when they found out that the complication rates of the allografts are significantly high. They provide the advantages of biological reconstruction leading to better functional outcomes and also provide the advantage of immediate stability

of the endoprosthesis. However results have shown that this prosthesis also carries the high complication rates associated with the allografts. [21]

TECHNIQUES FOR REPAIR OF THE EXTENSOR MECHANISM

Various techniques have been described in the literature for reconstruction of the extensor mechanism at the knee joint. The degree of surgical resection and also the type of prosthesis used for reconstruction influence the choice of extensor mechanism reconstruction. No randomised trials exist to compare the various methods of extensor mechanism reconstruction. The reconstruction options available according to the prosthesis used are described briefly below.

A. Classic endoprosthesis

Endoprosthesis are a popular means of reconstruction. The main problem with the use of the endoprosthesis is the need to attach the patellar tendon to the metal prosthesis. Various techniques have been described to overcome this problem.[22]

(a) Direct Fixation: Horowitz et al[23] presented a series of 16 patients and in 10 patients the reconstruction of the extensor mechanism was done by coronally splitting the patella and quadriceps tendon and the remnant patella was directly attached to a porous area on the anterior surface of the prosthesis. Functional assessment of 6 of these patients revealed an extensor lag of less than 20^{0} in 4 of these patients. However the direct fixation is associated with a high rate of complications and the 8 year follow up of this series revealed that 60% of these patients had revision or amputation as a result of the complications.

(b) Synthetic soft tissue augments: Many studies have reported the use of textile implants such as Dacron tapes, Trevira tube to fix the patellar ligament remnant to the prosthesis. [24, 25]

The Trevira tube was introduced for extensor mechanism reconstruction by Goshegeret al.[26] 'Ligament Advancement Reinforcement System (LARS®)' which is essentially a polyester ligament used to repair the defect in the patellar ligament and is secured to the prosthesis at the level of tibial tuberosity and also distally at the level of the prosthesis and tibial end interface.[27] Excellent or good functional results were achieved in 59% of the patients but ligament failure was seen in 23% (5 patients).

Fig 3. Modular endoprosthetic system Munich-Luebeck, EskaOrthodynamics GmbH, uebeck, Germany with the tibial fixation device for the double-layered Trevira cord[24]

(c) 'Biological' augmentation with or withoutsynthetic materials

Bickels tried to overcome the lack of healing of the attachment of the extensor apparatus by doing a biological fixation.[25] He used a Dacron® tape to secure the patellar tendon to the prosthesis. He used autologous bone graft to pack the patellar tendon and prosthesis interface and covered it with medial gastrocnemius muscle flap. This provided certain advantages: immediate mechanical fixation, biological reinforcement to the extensor mechanism, and vascularised tissue coverage to minimise infection and facilitate healing.

The biological reinforcement done undergoes osseointegration to the underlying porous-coated surface of the endoprosthesis. At 12 weeks a layered tendon – fibrocartilage – bone interface can be seen which resembles a normal tendon insertion. Quality of repair was also robust with few patients requiring secondary procedures for reinforcement.

Kotz and Coombs[22] reported the use of pedicled fibular graft for attachment of the patellar tendon and reconstruction with an endoprosthesis. This provides an advantage of doing a biological reconstruction without the use of synthetic material. The fibular graft was based on the peroneal vessels and attached to the tibial mid-shaft using screws and its proximal end was attached to the patellar tendon.

B. Allograft–endoprosthesis composites

Though theoretically the composite prosthesis are an attractive option, the high rates of failure of the allograft and subsequent failure of the extensor mechanism is discouraging. This method of reconstruction is also plagued by a high rate of infection. Donato reported an infection rate of 25%.[22]

C. Biologic reconstruction

Allograft allows direct attachment of the tendons and the ligaments to provide good functional outcome. Host patellar tendon is directly attached to the allograft. This can be reinforced with muscle flap to minimise the chances of infection and helps in healing. Excellent functional outcomes have been reported. In a case series of 34 cases of proximal tibial reconstruction using allograft by Ayerzaet al.[22] they found that the reconstructed tendon was stable in all patients at a mean follow up of 52 months. 24 patients had no extensor lag and the remaining 10 had a mean lag of 6.5^{0} . However this technique has a very high

complication rate. Clohisy et al reported that 15 of the 16 allografts for the proximal tibia had complications and 7 required removal.[22]

Muscle Flaps

The muscle flaps provide the soft tissue coverage for the prosthesis. This reduces the risk of infection, facilitates healing and also provides a mechanism for reconstruction of the extensor mechanism. Muscle flaps, in particular the pedicled gastrocnemius flap has been very popular. This was first used by Dubousset et al. This can be usedas a muscle or a myocutaneous unit. He described two techniques. The first one in which the patellar tendon was intact the medial gastrocnemius was transposed anteriorly and sutured to the tendon. Here the muscle is not divided at either the proximal or the distal end. In a situation where the patellar tendon is deficient the medial gastrocnemius was divided at its distal end and swung anteriorly and fixed to the underlying fibula and attached to the patellar tendon.[22]Malawer described a technique in which the medial gastrocnemius was rotated over the defect and sutured to the borders of the anterior muscles providing a soft tissue cover over the prosthesis.[28] Other flaps described are a combination of gastrocnemius flap and the semitendinosus tendon autograft, sartorius, biceps femoris, semitendinosus and latissimusdorsi muscle flap.

MATERIALS AND METHODS

Forty one proximal tibialosteosarcoma patients underwent limbsalvage in cancer institute between 2001 and 2011.The case records of these patients were reviewed and followed up for Quality of life assessment after limb salvage surgery.

EVALUATION

Patients suspected of having bone sarcoma were evaluated with X-ray and MRI of the local affected part. Metastatic work up was done with Chest X-Ray, CT Chest and Tc99 bone scintigraphy. The outside slides and paraffin blocks were procured for patients who had undergone biopsy outside. Jamshidi needle biopsy was done at the institute for patients who didn't have a biopsy done outside.

Tumours are staged according to the 7th edition of the AJCC cancer staging manual[29]

Primary tumour (T)

TX – Primary tumour cannot be assessed

T0 – No evidence of primary tumour

T1- Tumour 8 cm or less in greatest dimension

T2- Tumour more than 8 cm in the greatest dimension

T3- Discontinuous tumours in the primary bone site

Regional lymph nodes (N)

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph nodal metastasis

N1 – Regional lymph nodal metastasis

Distant metastasis (M)

M0 – No distant metastasis

M1a – Lung metastasis

M1b – Metastasis to other distant sites

Histological grade (G)

GX – Grade cannot be assessed

G1 – Well differentiated – low grade

G2 – Moderately differentiated – low grade

G3 – Poorly differentiated

G4 – Undifferentiated

STAGE GROUPING

STAGE	T	N	M	G
IA	T1	N0	M0	G1, G2, GX
IB	T2	N0	M0	G1, G2, GX
	T3	N0	M0	G1, G2, GX
IIA	T1	N0	M0	G3, G4
IIB	T2	N0	M0	G3, G4
III	T3	N0	M0	G3, G4
IVA	Any T	N0	M1a	Any G
IVB	Any T	N1	Any M	Any G
	Any T	Any N	M1b	Any G

NEO-ADJUVANT CHEMOTHERAPY

Neoadjuvant chemotherapy with ifosphamide, adriamycin and cisplatin were given for two cycles and the response to chemotherapy was assessed clinically and if necessary radiological with MRI. If the patient was found to be a candidate for limb salvage then a scanogram of the affected limb was taken and depending on the dimension of the tumour, the bone scan length of the lesion and the dimensions of the remaining bone the custom made prosthesis design was prepared and ordered for fabrication.

Fig 4. Custom made megaprosthesis made of titanium alloy with the grooves for insertion of the prolene mesh

SURGERY

Surgery is usually performed after 3 to 4 cycles of neo-adjuvant chemotherapy, depending on the response to the neo-adjuvant therapy. Repeat imaging is done for reassessment of the borderline resectable tumours. Limb salvage surgery is done with custom made mega-prosthesis.

Surgicalprinciples:

Adhering to the surgical principles of limb salvage and maintaining thorough aseptic precautions at each phase of the surgery isthe key for the successful outcomes and avoiding preventable complications. It includes thorough pre-surgical scrub with antiseptic solution the day before and on the day of surgery and after induction of anaesthesia.

Incision:

Incision is placed on the medial aspect starting at the lower end of the femur and extended across the knee joint to the middle or lower third of the leg. Incision should include the previous biopsy scar. Thick fasciocutaneous flaps are raised

Popliteal vessel dissection :

Early popliteal exploration is the key to assess the resectabilty of the tumor.

Popliteal space and trifurcation of the popliteal artery is exposed by dissection. Care should be taken to preserve the vascular supplyto the medial gastrocnemius which is by the medial sural artery which goes in a posteromedial direction to the geniculate artery. Further vascular dissection is done by and dividing the medial gastrocnemius insertion and splitting the soleus muscle.

Knee joint exposure:

The capsule is incised circumferentially 1 cm away from the tibia and the patellar tendon. The cruciate ligaments are visually exposed and transected and the knee joint is opened.

Peroneal nerve exposure and tibiofibular joint resection:

Lateral fasciocutaneous flap is raised to expose the proximal fibula and the peroneal nerve.The tibio-fibular joint is resected en-bloc along with the tumour.

Bone cuts:

Distally tibia is transected 3 to 4 cm from the bone scan uptake margin and proximally articular plate of femur is transected and the specimen is removed enbloc.

Fixation of prosthesis:

Cut ends of the bone are reamed with reamer to accommodate the prosthesis. Bone cement (PMMC) is used to fix up the tibial prosthesis in position after checking the alignment.

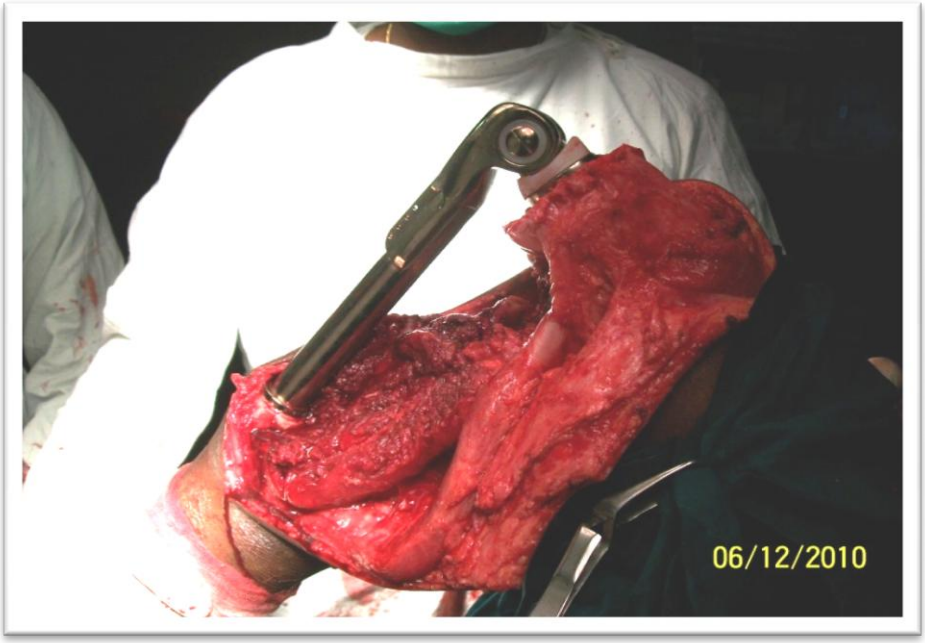


Fig 5. Fixing the prosthesis with bone cement after ensuring correct alignment

Soft tissue and Extensor reconstruction:

Extensor mechanism is reconstructed using prolene mesh anchored to the prosthesis and the patellar ligament using non absorbable suture material prolene. Medial gastrocnemius is mobilized to provide coverage for the prosthesis and mesh and sutured to the muscles in the anterior compartment.

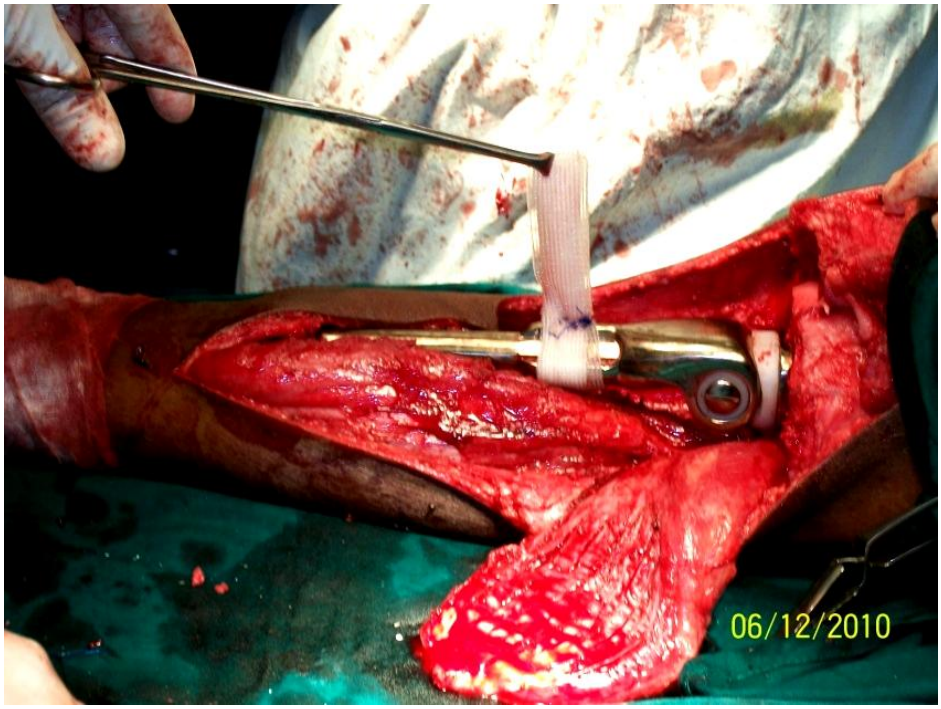


Fig 6. Fixing the prolene mesh to the prosthesis

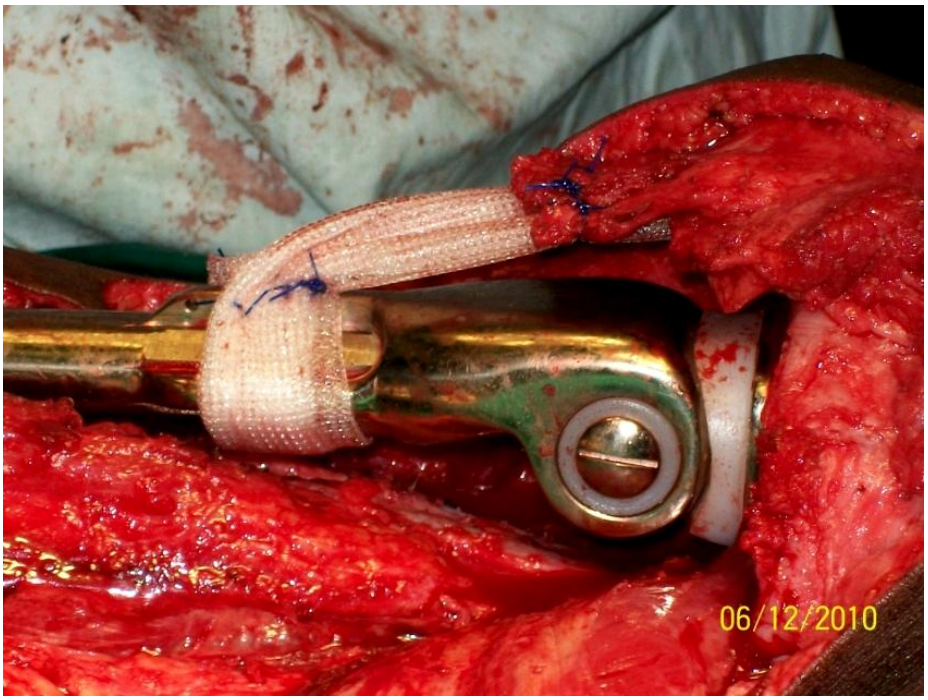


Fig 7. Fixing the prolene mesh to the distal end of the patellar tendon

Fig 8. Medial gastrocnemius muscle flap used to wrap around the prosthesis and the reconstructed extensor mechanism

Wound closure:

After ensuring complete haemostasis, suction drains are placed and majority of the wounds are closed primarily and some cases required skin grafting to achieve closure of the wound.

Rehabilitation

Patient's knee was kept extended to allow the reconstructed extensor mechanism to heal. Static quadriceps exercises are begun on day 7, non-weight bearing mobilization is begun at 2 to 3 weeks, weight bearing mobilization is begun at 4-6 weeks and full weight bearing is begun at 6-8 weeks. All the rehabilitation is done under the supervision by our physiotherapists.

FOLLOW UP

Patients after completion of treatment were followed up according to the institute protocol. Monthly in first year, two monthly in the second year, three monthly in the third year, six monthly in the fourth and fifth year and then annually. Every visit includes clinical examination, chest x-ray, physiotherapy. Quality of life assessment and extensor lag were measured after 6 months of the procedure. Further investigation were done as clinical symptoms and sign warranted.

Extensor lag measurement:

To measure the extensor lag the patient was put in a high sitting posture and using a goniometer the range of movements and the lag in extension from full extension was measured.

Fig 9.Measurement of the extensor lag using a goniometer.

COMPLICATIONS AND ITS MANAGEMENT

Patients after limbsalvage surgery face with varieties of complication and they were managed appropriately. Marginal skin necrosis was managed mostly by conservative treatment rarely

some required debridement and secondary suturing, skin grafting or local flaps. Major complications were approached with redoprosthesis for prosthesis fracture, prosthesis removal or amputation for prosthesis infection, amputation for local recurrence and metastectomy for resectable lung metastasis in a patient with good performance status and adequate disease free survival.

ASSESSMENT OF THE QUALITY OF LIFE AND FUNCTION OUTCOME

Functional outcome assessment was done using the musculoskeletal tumour society scoring system (MSTS)[30] and Quality of life by Cancer Institute Quality of life Questionnaire Version II[31].

Scoring system – International society of limb salvage

SCORE	PAIN	FUNCTION	EMOTIONAL ACCEPTANCE	SUPPORTS	WALKING ABILITY	GAIT
5	None	No Restriction	Enthuse	None	Unlimited	Normal
4	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
3	Moderate	Restriction in recreational activities	Satisfied	Brace	Limited	Minor cosmetic
2	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
1	Moderate	Partial disability	Accepts	One cane or crutch	Household	Major cosmetic, minor handicap
0	Severe	Total disability	Dislikes	Two canes or crutches	Unable to walk unaided	Major cosmetic, minor handicap

Cancer Institute QOL questionnaire[31] consisted of 42 variables and the maximum score was 180. Higher the score better the quality of life. The interpretation of the QOL II version is as follows:

1. <99 – Significantly poor

2. 99-117 – Below average

3. 118-146 – Average

4. 147 – 165 – Above average.

5. >165 – significantly high

STATISTICAL ANALYSIS

Statistical analysis was done by SPSS 17 (SPSS software Inc USA). Extensor lag and quality of life assessment were analysed by T –test.

RESULTS

41 consecutive patients who underwent limb salvage surgery for proximal tibial osteosarcomas from 2001 to 2011 were analysed.

Mean age of the patients was 17.7 years (range 9-35 years). There were 15 patients with age more than 18 years and 26 patients with age up to 18 years.

29 patients (70.7%) of the patients were male and 12 patients (29.3%) were females.

J needle biopsy was used for the diagnosis in 32 patients (78%) and open biopsy was performed in 9 patients (22%). Of note, no open biopsies were performed in our institute. All of the 9 open biopsies were done outside and the slides were reviewed here.

Preoperative biopsy was the follows

Histiology	Frequency
Classical osteosarcoma high grade	19
Chondroblastic osteosarcoma	8
Pleomorphic sarcoma	11
Fibroblastic osterosarcoma	1
Giant cell tumour of bone	1
Chondrosarcoma	1

The average bone scan length was 13.5 cms and 30 patients had bone scan length of up to 15 cms and 11 patients had bone scan length more than 15 cms.

CT chest done upfront showed nodules in the chest in 4 patients. Among these patients 3 had solitary pleural based nodule and 1 patient has 2 nodules. However only one patient among

the three with solitary nodule in the chest developed lung metastases after limb salvage with a DFS of 20.2 months and he underwent metastectomy twice. His overall survival was 70.1 months.

Neoadjuvant chemotherapy was given in all but 2 patients. These two patients had a preoperative diagnosis of giant cell tumour of the bone and chondrosarcoma respectively. 32 patients received either 3 or 4 cycles of neoadjuvant chemotherapy. 7 patients received either 5 or 6 cycles of neoadjuvant chemotherapy.

16 patients underwent reconstruction with endoprosthesis and myoplasty (gastrocnemius muscle flap) and 25 patients underwent reconstruction with mesh-myoplasty (using prolene mesh for reconstruction of the extensor mechanism). 31 patients had resection of the fibular head and 22 patients had ligation of the anterior tibial artery during resection of the tumour. 6 patients needed SSG cover during the procedure.

Early complication

Complications occurring within 30 days of the surgery were considered as early complications.

Early complication	Frequency	Treatment
Foot drop	14	Conservative
Skin necrosis	6	Conservative (2), flap cover (1) and secondary suturing (3)
Foot drop and skin necrosis	1	Conservative

Over all 51.2% patients had early minor complications. However about 50% of them were foot drops which recovered in most of the patients. None of them had any major complication in the early postoperative period for which removal of prosthesis was necessary.

Complications occurring after 30 postoperative days were considered as late complications. Over all 10 patients had late complications (24.4%).

Late complication	Frequency	Treatment
Infection	3	Prosthesis removal (2) Amputation (1)
Fracture prosthesis	2	Redoprosthesis (1) Patient was not willing for redoprosthesis (1)
Aseptic loosening	3	Redoprosthesis (3)
Exposed prosthesis	1	Prosthesis removal
Fracture of the limb proximal to the prosthesis	1	Open reduction and internal fixation

Post-operative histopathology

Histology	Frequency
Classical osteosarcoma	23
Chondroblastic osteosarcoma	9
Pleomorphic sarcoma	1
No residual tumour	7
Giant cell tumour rich osteosarcoma	1

Tumour necrosis:

Percentage of necrosis in the post-operative specimen was examined

Percentage of necrosis	Frequency
$>90^0$	9 (22%)
0^0 to 90^0	32 (78%)

Recurrence:

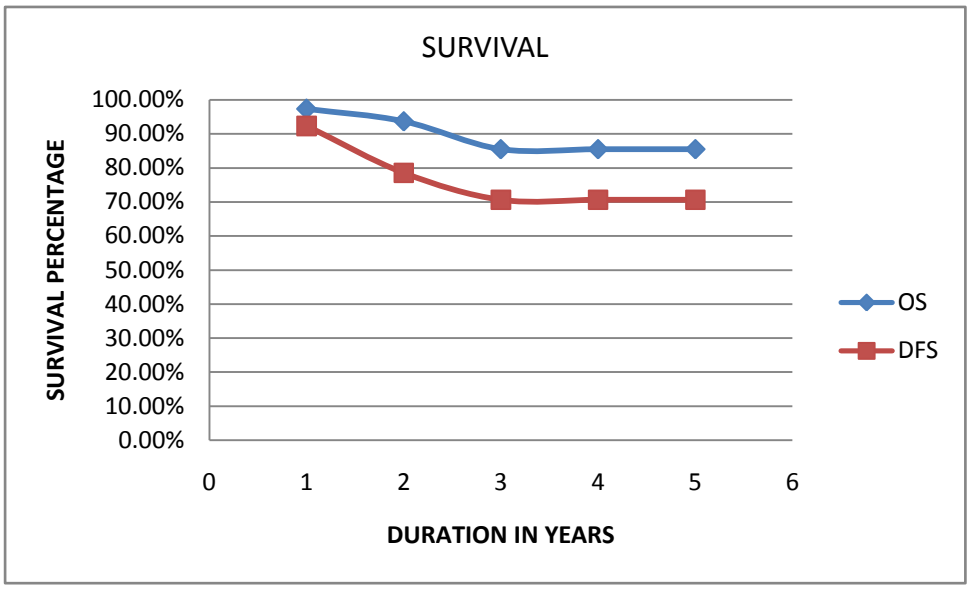
10 patients (24.4%) had recurrence on followup.

Site of recurrence	Frequency
Local	1
Distant	8
Local and distant	1

Overall only 2 patients (4.8%) had local recurrence and 9 patients (21.95%) had lung metastasis. The patient with both local and distant recurrence was offered only supportive care. The patient with only local recurrence defaulted for evaluation. Of the 8 patients with only distant metastasis 6 were offered supportive care (due to multiple bilateral metastasis)and 1 patient underwent metastectomy twice and had chemotherapy. The other patientunderwent metastectomyonce.

Survival analysis was done using SPSS 17.0 version and Kaplan Meyers analysis.

5 years overall survival and disease free survival were 85.5% and 70.6% respectively. In both the overall survival and the disease free survival the events occurred during the first 2 years. The mean overall survival was 38 months and mean disease free survival was 34 months.

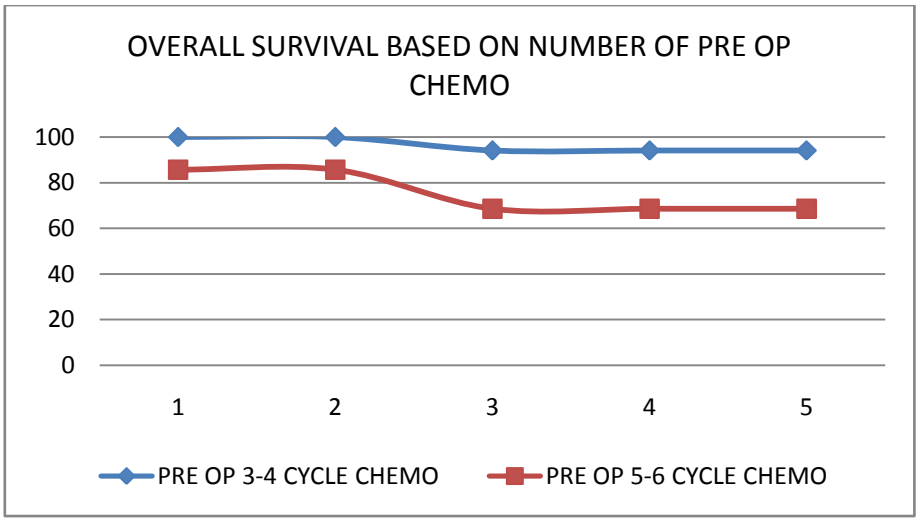


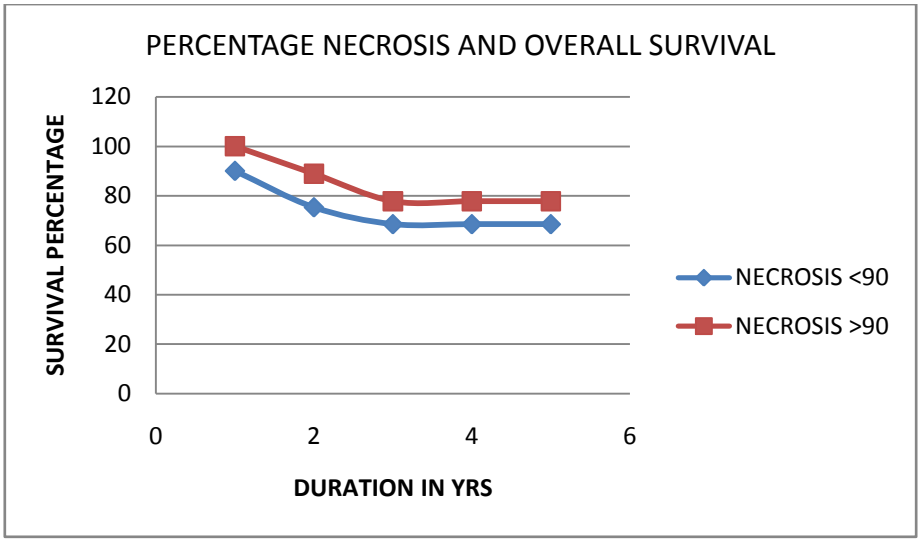
Factors like age of the patient, type of biopsy, bone scan length of the lesion, number of preoperative chemotherapy cycles, type of surgery and amount of necrosis in the post-operative specimen were evaluated for impact on survival.

Among these there was a statistically significant difference in survival only in patients receiving 3 to 4 cycles of neo-adjuvant chemotherapy versus those receiving 5 to 6 cycles of neo-adjuvant chemotherapy with the 5 year overall survival being 94.1% versus 68.6% respectively

(p= 0.045)

S.No	Variable	5 year overall survival in %	p value
1.	Age upto 18 years	81.4	NS
	Age > 18 years	93.3	
2.	Bone scan length upto 15 cms	85.7	NS
	Bone scan length >15 cms	90.9	
3.	J needle biopsy	84.3	NS
	Open biopsy	87.5	
4	3 to 4 cycles pre op chemo	94.1	0.045
	5 to 6 cycles pre op chemo	68.6	
5	Myoplasty	86.7	0.885
	Meshmyoplasty	84.7	
6	Necrosis upto 90%	84.6	NS
	Necrosis >90%	87.5	





Disease free survival:

Similarly these factors were analysed for any influence on the disease free survival.

S.No	Variable	5 year Disease free survival in%	p value
1.	Age upto 18 years	64.8	NS
	Age > 18 years	80	
2.	Bone scan length upto 15 cms	64.3	NS
	Bone scan length >15 cms	90.9	
3.	J needle biopsy	75.5	NS
	Open biopsy	53.3	
4	3 to 4 cycles pre op chemo	76.9	NS
	5 to 6 cycles pre op chemo	53.6	
5	Myoplasty	80.8	NS
	Meshmyoplasty	62	
6	Necrosis upto 90%	68.5	NS
	Necrosis >90%	77.8	

Prosthesis survival:

The mean prosthesis survival was 34.5 months (range 2.3 months to 133.1 months). The 5 year prosthesis survival was 86.5%. All of the prosthesis failures occurred in the first 3 years. Prosthesis survival was analysed with respect to bone scan length, type of surgery (myoplasty versus meshmyoplasty), depending on the type of the biopsy and whether the patient received 3 to 4 or 5 to 6 cycles of pre-operative chemo.

S.No	Variable	5 year prosthesis survival in%	p value
1.	Bone scan length upto 15 cms	89.8	NS
	Bone scan length >15 cms	85.7	
2.	J needle biopsy	88.7	NS
	Open biopsy	77.8	
3.	3 to 4 cycles pre op chemo	89.3	NS
	5 to 6 cycles pre op chemo	71.4	
4	Myoplasty	93.8	NS
	Meshmyoplasty	79.9	

There was no statistically significant difference in the prosthesis survival between the cases that underwent myoplasty and meshmyoplasty.

Quality of life assessment:

Quality of life assessment was done based on the Cancer Institute QOL questionnaire II for cancer patients[31]and the MSTS scoring system[30] was used for the functional outcome.

Of the 41 patients 4 of the patients were lost to follow-up and were not available for QOL assessment. 2 patients died and 2 patients had their prosthesis removed before the time of QOL assessment. So QOL was done for 33 patients and among these 24 had undergone meshmyoplasty and 9 had undergone myoplasty. Following are the results of the analysis.

QOL Variable	Myoplasty	Mesh-myoplasty	p Value using T test
QOL total	148.89	144.17	0.197
General well being	25.78	23.71	0.075
Physical well being	37.11	36.0	0.139
Psychological well being	23.89	24.71	0.627
Interpersonal relationship	15.44	14.63	0.207
Sexual and personal ability	4.78	4.50	0.713
Cognitive well being	11.00	11.21	0.642
Optimism and belief	7.67	7.50	0.599
Economical well being	8.78	8.67	0.875
Information support	7.56	6.46	0.035
Patient physician relationship	4.00	3.88	0.414
Body image	2.89	2.92	0.937

QOL analysis between the two type of surgeries i.e. myoplasty and mesh-myoplasty did not show any statistically significant outcomes in the overall quality of life. However theover all QOL was slightly better in the analysis done for information support. Information support was concerned with the amount of information the patient expected and the amount of information the patients were able to get from the doctors.

Functional outcome was assessed using the MSTS scoring system[30]

A total of 6 factors were analysed and the following are the results.

MSTS variable	Myoplasty (mean)	Mesh-myoplasty (mean)	p Value using T test
PAIN	4.78	4.67	0.599
FUNCTION	3.56	3.33	0.479
EMOTIONAL ACCEPTANCE	2.89	3.50	0.031
SUPPORTS	4.44	4.54	0.748
WALKING ABILITY	3.56	3.29	0.397
GAIT	3.11	3.04	0.805
TOTAL	22.33	22.38	0.964

This shows that the overall functional outcome between the patients undergoing myoplasty and mesh-myoplasty was similar. However when the patients were analysed based on the emotional acceptance of the patients, the patients undergoing mesh-myoplasty showed a statistically better outcome (p=0.031) than the group undergoing myoplasty.

EXTENSOR LAG ANALYSIS

Extensor lag was measured for 32 patients (8 with myoplasty and 24 with meshmyoplasty). 4 patients were lost to follow up, 3 patients were dead and 2 patients had their prosthesis removed due to infection prior to the time when the extensor lag was measured.

The mean extensor lag in the patients undergoing myoplasty was 68.13^0 and the mean extensor lag in the patients undergoing mesh-myoplasty was 36.66^0 and the difference was statistically significant (p=0.004).

Type of surgery	0^0	$1^0 – 20^0$	$21^0 – 50^0$	$51^0 – 70^0$	$>70^0$
Myoplasty	0	0	1	3	4
Mesh-myoplasty	2	5	13	1	3

None of the patients in the myoplasty arm had an extensor lag of less than 21^0 . Whereas 2 patients with mesh-myoplasty had 0^0 extensor lag.

DISCUSSION

The management and the outcomes including the survival and the functional outcomes of proximal tibial osteosarcomas has changed considerably due to the use of chemotherapy, use of advanced imaging technology and refinements of surgical techniques. The prosthesis survival also has increased due to use of better quality and designing of prosthesis. Endoprosthetic reconstruction is now the preferred method used for reconstruction with various methods used for reconstruction of the extensor mechanism which is one of the important factors affecting the functional outcomes.

In our study we included 41 consecutive cases of proximal tibial osteosarcomas who underwent limb salvage surgery at our institute from 2001 to 2011 with a mean follow up of 38 months.

The mean age of the patients was 17.7 years (range 9-35 years). There were 15 patients with age more than 18 years and 26 patients with age up to 18 years. In the German-Austrian-Swiss co-operative study group comparison of the overall survival of the patients with age of the patients <40 years and >=40 years showed statistically significant difference in favour of the group less than 40 yrs of age

Our study did not show any statistically significant difference in the age group =< 18 years and > 18 years.

Generally many studies have shown that proximal tibial osteosarcomas are a favourable sub-site for the sarcomas[19, 32].

The Cooperative German-Austrian-Swiss Osteosarcoma Study Group[32] in their analysis of 1702 cases of osteosarcomas found that the tumours in the proximal tibia had a 5year and 10 year overall survival of 77.5% and 72.0% respectively, whereas the overall survival in the entire group for 5 years and 10 years was 65.3% and 59.8%.

In the Brazilian osteosarcoma treatment group studies III and IV by SérgioPetrilliet al[34], they found that the overall 5 and 10 year survival was 50.1% and 46.7% whereas it was 60.0% and 56.7% respectively for tumours arising in the proximal tibia

However in our study we have included only cases which had small volume tumours with better prognosis and who have undergone limb salvage surgery where as the other studies quoted have included cases with metastasis and also patients who have undergone amputation.

Various studies have shown that the outcomes with larger tumour volumes have been poorer[32, 33]. In our study we used the bone scan length of the tumour to classify them into 2 categories. They were classified as tumour with bone scan length =<15 cms (30 patients – 73.2%) and tumours >15 cms (11 patients – 26.8%). We did not find any statistically significant difference in the survival in these two subgroups.

If patients are having extensive soft tissue component then it is one of the relative contraindications to performing limb salvage surgery. Spanier et al. from the University of Florida have extensively studied the effect of local extent of the tumour on disease free survival and overall survival.[35]

They studied the effect of the local tumour extent on the disease free survival. They included 51 patients with Enneking stage IIB tumours. They classified the tumours into 6 types depending on the local extent of the tumour.

E1 – Tumour only touches the periosteum but does not elevate or penetrate it.

E2 – Tumour touches and elevates the periosteum but does not penetrate it.

E3 – Tumour penetrates into the periosteum but does not penetrate through the periosteum.

E4 – Tumour penetrates through the periosteum with minimum extraperiosteal extension without invasion of another structure (like muscle, tendon or ligament)

E5- Tumour invades one additional structure

E6 – Tumour invades two or more additional structures.[35]

They found that the risk of failure was 5.9 times higher if tumour involed 2 or more surrounding tissues compared to the other subgroups.[35]

Study	Size of the tumour	OS	p Value	DFS	p Value
German-Austrian-Swiss group[32]	< one third	72.1%	<.0001	61.0%	<.0001
	>= one third	58.4%		42.9%	
Bacci et al[33] based on the tumour volume	=<150 ml			65%	NS
	>150 ml			52%	
SérgioPetrilli et al[34] -tumour length	=<12cms	64.5%	<.0001	48.1%	.009
	>12 cms	40.5%		30.4%	
Spanier SS, Shuster JJ, Vander Griend RA[35]	E1 – E5	82.3%		79.8%	
	E6	37.8%		17.6%	
Our study – Bone scan length	=<15cms	85.5%	NS	64.8%	NS
	>15 cms	64.3%		90.9%	

Chemotherapy

The use of chemotherapy has brought about a revolution in the outlook of these previously lethal tumours. The advantages of giving preoperative chemotherapy include:

1. Early initiation of the systemic therapy.

2. Borderline cases for limb salvage can undergo limb salvage surgery following tumour shrinkage after chemotherapy.

3. The response of the tumour to the chemotherapy can be assessed.

4. Provides time for designing and fabrication of the custom made prosthesis.

However the disadvantage is that the chemotherapeutic agent has to act against a large tumour burden.

Pediatric oncology group conducted a randomised control trial POG 8651, to compare the preoperative chemotherapy versus adjuvant chemotherapy. Of the 100 patients 45 underwent preoperative chemotherapy and 55 underwent straight surgery followed by chemotherapy. The 5 years DFS for undergoing immediate surgery and preoperative chemotherapy was 65% and 61 % (p -.8) and the rate of limb salvage for these groups were 55% and 50% respectively. It was concluded that chemotherapy was effective in both the settings[36]. In our study 2 patients did not receive a preoperative chemotherapy because the preoperative diagnosis for these patients was giant cell tumour of the bone in one case and chondrosarcoma in the other case. As the number of cases undergoing immediate surgery was very less statistical analysis couldn't be done.

The response to neo-adjuvant chemotherapy has been an important prognostic factor for the overall and the disease free survivals. Several centres have developed criteria to

evaluate the chemotherapy response. Huvos et al. at MSKCC[37], Salzer-Kuntschik et al.[38] (system used by the COSS study group) and Picci et al [39] at InstitutiOrthopedico Rizzoli independently developed criteria to assess the tumour response to chemotherapy. But as a consensus a tumour response >90% is taken as good response and =<90% is taken as poor response.

Using this criterion the chemotherapy response was assessed in our study and 30 patients (76.92%) were poor responders and 9 (22%) were good responders.

Response to chemotherapy has been reported by various studies and has been a statistically significant predictor of survival[32, 34, 40]. However the update by Bacciet al[33] did not show any statistically significant difference in the outcomes of poor responders to chemotherapy compared to the good responders.

Huvos et al[37]		Salzer-Kuntschik et al.[38]		Picci et al [39]	
IV	No histologic evidence of viable tumor	I	No viable tumor cells	Good response	90%-99% tumor necrosis
III	Only scattered foci of viable tumor cells	II	Single viable tumor cells or cluster <0.5 cm	Fair response	60%-89% tumor necrosis
II	Areas of necrosis due to chemotherapy with areas of viable tumor	III	Viable tumor<10%	Poor response	<60% tumor necrosis
I	Little or no chemotherapy effect	IV	Viable tumor 10% - 50%		
		V	Viable tumor>50%		
		VI	No effect of chemotherapy		

Response to preoperative chemotherapy and survival outcomes

Study	Disease free survival		p value	Overall survival		p value
	Good responders	Poor responders		Good responders	Poor responders	
COSS study[32]	67.6%	38.6%	<.0001	77.8%	73.4%	<.0001
SigbjornSmeland et al[40]	89%	53%	.004			
Bacci G[33]	62%	51%	NS			
Our study	68.5%	77.8%	0.539	87.5%	84.6%	0.521

Even though our study did not reveal a significant difference in the survival of the patients with poor response to preoperative chemotherapy compared to the patients with good response, the survival curves never met and may be with more number of patients or a longer follow up we may be able to appreciate a difference in survival between these subgroups.

We also analysed the survival of the patients who had received 3 to 4 cycles of preoperative chemotherapy versus those receiving 5 to 6 cycles of preoperative chemo. We found that patients receiving 3 to 4 cycles of chemotherapy had a statistically significant better overall survival (94.1% versus 68.6% with p = .045) compared to the patients who received 5 to 6 cycles of chemotherapy.

We also analysed the survival outcomes with respect to type of surgery (myoplasty v/s meshmyoplasty), whether the fibular head was resected or not, whether the anterior tibial artery was ligated or not and also depending on the type of biopsy (J needle biopsy versus open biopsy). The survival outcomes between the above compared subgroups were not different statistically.

Recurrences

There were 10 cases of recurrence in our series. 1 patient had local recurrence, 1 patient had both local recurrence and distant metastasis and 8 patients had lung metastasis. The mean duration for recurrence or metastasis was 14.97 months (range 4.9 to 26.3 months). The local recurrence rate was 4.8% (2 patients) and the distant recurrence rate was 21.95% (9 patients). Most of the published series for limb salvage surgery have documented involved margins, larger size of the tumour, open biopsy, local response to chemotherapy and low volume centres as significant predictors for local recurrence. [41, 42, 43, 44, 40, 34]

In our study none of the patients had margin positivity and as the number of local recurrences was only 2 statistical analyses couldn't be done.

Our local recurrence rates are comparable with the major published series.

Study	Local recurrence rate
P. Picci et al[41]	7%
D. Andreou et al[42]	5.6%
Sigbjorn Smeland[40]	4%
A. Sérgio Petrilli[34]	10%
Torbert, Jesse T MD et al[43]	6.8%
Bacci G et al[44]	6%
R. J. Grimer, et al.[9]	12.6%
Our study	4.8%

Prosthesis survival

The mean prosthesis survival was 34.5 months (range 2.3 months to 133.1 months). The 5 yr prosthesis survival was 86.5%. All of the prosthesis failures occurred in the first 3 years. Prosthesis survival was analysed with respect to bone scan length, type of surgery (myoplasty versus meshmyoplasty), depending on the type of the biopsy and whether the patient received 3 to 4 or 5 to 6 cycles of pre-operative chemo. There was no statistically significant difference in the above compare subgroups.

Our prosthesis survival of 86.5% is comparable to the various studies quoted in the literature regarding the prosthesis survival.

Study	Proximal tibial Prosthesis survival	
	5 years	10 years
MayilVahananNatarajan et al.[45]	85.5	
Adam J. Schwartz MD et al.[46]	93.8%	86.5%
G. J. C. Myers[20] (fixed hinge)	68%	39%
G. J. C. Myers[20] (rotating hinge)	88%	75%
Flint et al.[47] (fixed hinge)	73%	
Wu et al[48] (custom prosthesis)	44.4%	22.2%
Wu et al[48] (modular prosthesis)	81.4%	65.3%
Our study (over all)	86.5%	
Our study (myoplasty)	93.5%	
Our study (meshmyoplasty)	79.9%	

Even though the 5 yr prosthesis survival was better in the myoplasty arm it did not reach statistical significance. The 8 year prosthesis survival was 64.3% for the myoplasty arm and 79.9% for the meshmyoplasty arm. Most of the events have occurred in the first 3 years. However we need a longer follow up with the meshmyoplasty arm to clearly tell us about the long term outcomes.

Complications

Early complications were taken as the complications occuring within 30 days of the surgery. Of the 41 patients 14 patients had a temporary foot drop which recovery in all but 2 of the patients on followup. 6 patients has mariginal skin necrosis which was managed conservatively in 2, by flap cover in 1 and with secondary suturing in 3 patients. 1 patient had both foot drop and marginal skin necrosis and was managed conservatively

Late complications were taken as those occuring after 30 days of the surgery. In our series 10 patients (24.4%) had late complications. The following were the complication breakdown and the treatment given for them.

Late complication	Frequency	Treatment
Infection	3 (7.31%)	Prosthesis removal (2) Amputation (1)
Fracture prosthesis	2 (4.87%)	Redoprosthesis (1) Conservative treatment(1)
Aseptic loosening	3 (7.31%)	Redoprosthesis (3)
Exposed prosthesis	1 (2.43%)	Prosthesis removal
Fracture of the limb proximal to the prosthesis	1 (2.43%)	Open reduction and internal fixation

In most of the series reported on proximal tibial prosthesis, infection and aseptic loosening has been stated as most common causes for prostesis failure.

Here we compare the infection rates, asceptic loosening rates and prosthesis loosening rates of our study with the other studies stated in literature.

Study		Infection	Asceptic loosening	Fracture prosthesis
Our study		7.31%	7.31%	4.87%
R. J. Grimer, et al.[9]	With gastrocnemius	12%	-	3.31% (5/151)
	Without gastrocnemius	36%		
P. S. Unwin et al.[19]		36.58%	19.51%	4%
Jacob Bickels et al[25]		3.6%	-	3.63%
Myers et al[20]	Fixed hinge	19.5%	46%	1.92%
	Rotating hinge		3%	
Flint MN et al[47]	Uncemented prosthesis	15.9%	0%	4.54%
Adam J. Schwartz et a.l[46]		5.8%	11.53%	
MayilVahananNatarajan et al.[45]		12%		
Wu CC et al.[48]		15.9%		
Horowitz et al.[23]		37.5%		

The major complications in the proximal tibial prosthesis are infection, aseptic loosening and fracture of the prosthesis stem. Infections rates have come down with the use of adequate soft tissue cover, basically used is the medial gastrocnemius muscle flap.

Aseptic loosening of the prosthesis is another complication in which the use of prosthesis with a rotating hinge has reduced the incidence. Recent reports of using uncemented prosthesis have also reported a reduction in the rates of aseptic loosening.

So these technical modifications have reduced the complication rates in this anatomical site which traditionally has a higher complication rate.

Quality of life assessment

QOL was analysed by the Cancer Institute QOL Questionnaire[31] which is based on 42 questions and based on that scores are given. Higher the scores better the QOL.

The score of the patients undergoing myoplasty was 148.89 which is just above the average score, and the score of the patient undergoing mesh-myoplasty was 144.17 which is in the higher range of average scores. There was no statistically significant difference in the quality of life of the patients undergoing myoplasty or mesh-myoplasty.

None of the factors subgrouped to denote different aspects of the quality of life showed any difference in the two groups except the aspect of information support.

Over all the quality of life was satisfactory.

Functional outcome assessment.

Functional outcome was assessed using MSTS scoring system[30]. The mean MSTS score was 22.35 (74.5%). It was 22.33 in the patients undergoing myoplasty and 22.38 in the

patients undergoing mesh-myoplasty. Comparison of the functional outcome between the two groups was not statistically significant. However while analysing the scores concerned with 'emotional acceptance' there was a statistically significant difference in favour of the group in which the reconstruction was done using mesh-myoplasty.

The MSTS score of our series was comparable with those in the other series.

Study	MSTS score
R. J. Grimer, et al.[9]	77%
Vijay Titus MS[49]	82.1%
Adam J. Schwartz MD et al.[46]	82%
Zhang Y.[50] (tibiofibular joint involved)	70%
Flint MN et al[47]	75%
Our study	74.5%

As compared above the functional outcomes of the patients in our series is satisfactory.

Extensor lag

The active extensor lag for the patients undergoing myoplasty was $68.13^0$and for the patients undergoing mesh-myoplasty was 38.81^0. The difference in the outcomes was statistically significant in favour of the group undergoing mesh-myoplasty (p=0.004). No revision surgeries were done in our surgeries for the repair of the extensor mechanism. The following table compares the outcomes of the extensor lag of our series with that of other series.

Study	Mean Extensor Lag
Our study (myoplasty)	68.13^0
Our study (mesh-myoplasty)	38.81^0
R. J. Grimer, et al.[9]	30^0
Adam J. Schwartz MD et al.[46]	17.9^0
Flint MN et al[47]	6^0
Vijay Titus MS[49]	4^0
Dominkus M[27]	25^0
Gosheger G[26]	7.5^0
Shimose S[51]	26^0

Though the extensor lag in the mesh-myoplasty arm in our series was significantly better than the arm which underwent myoplasty alone, it was more than some of the other studies. The extensor lag in our series could be further improved by

1. Considering revision surgery for the extensor mechanism for patients with poor extension.

2. Extensor mechanism could be augmented with bone grafts, wire cerclage, etc.

CONCLUSION

1. With the use of effective modern chemotherapy osteosarcoma treatment has seen a paradigm shift. Excellent survival results are seen in the proximal tibial osteosarcomas in our study which is at par with the international studies. Patients receiving 3 to 4 cycles of preoperative chemotherapy showed better survival outcome than those receiving 5 to 6 cycles of preoperative chemotherapy, thought it was not statistically significant. Good responders to preoperative chemotherapy also showed a trend towards better survival though it was not statistically significant.

2. Limb salvage surgery has been very satisfactorily done for the proximal tibial osteosarcomas, which is traditionally considered a difficult site to reconstruct.

3. Prosthesis survival at this site is influenced by a high rate of complications which include infection, prosthesis loosening and fracture of the prosthesis. The modifications of the surgical techniques and use of flaps for soft tissue cover has significantly reduced these complications.

4. There was no statistically significant difference in the prosthesis survival times of the patients undergoing myoplasty versus those undergoing mesh-myoplasty.

5. The extensor lag was significantly better in the patients undergoing mesh-myoplasty, but compared to international studies it was slightly inferior. We may need to consider the use of bone grafts augmentation for better bio-integration of the extensor mechanism.

BIBLIOGRAPHY

1. Peltier LF. Tumors of bone and soft tissues. *Orthopedics: A History and Iconography*. San Francisco, Calif: Norman Publishing; 1993:264-91

2. Mallon WJ. The registry of bone sarcoma. *Ernest Amory Codman: The End Result of a Life in Medicine*. Philadelphia, Pa: WB Saunders Co; 2000:107-21.

3. Link MP, Goorin AM, Miser AW, et al. The effect of adjuvant chemotherapy on relapse-free survival in patients with osteosarcoma of the extremity. *N Engl J Med*. Jun 19 1986;314(25):1600-6.

4. Rosen G, Murphy ML, Huvos AG, Gutierrez M, Marcove RC. Chemotherapy, en bloc resection, and prosthetic bone replacement in the treatment of osteogenic sarcoma. *Cancer*. Jan 1976;37(1):1-11.

5. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma.*ClinOrthopRelat Res*. Nov-Dec 1980;153:106-20.

6. Custom made megaprosthesis and limb salvage surgery by Prof Dr MV Natarajan.scripts.tnmgrmu.ac.in/vc/custommegaprosthesis.pdf

7. Huvos AG.*Bone tumors: diagnosis, treatment and prognosis.* Philadelphia,etc: WB Saunders Co, 1979.

8. Schajowicz F. *Tumors and tumorlike lesions of bone: pathology,radiology and treatment.* 2nd ed. Berlin, Springer-Verlag, 1994.

9. R. J. Grimer, et al. J Bone Joint Surg [Br] 1999;81-B:488-94.

10. Endoprosthetic reconstruction in LSS. www.sarcoma.org/publications/mcs/ch25.pdf

11. Picci P, Bacci G, Ferrari S et al. Local recurrence after limb salvage procedures for osteosarcoma: Correlation with margins and chemotherapy induced necrosis. J Bone Joint Surg 1993; 75(Suppl II): 211

12. Endoprosthetic reconstruction in LSS. www.sarcoma.org/publications/mcs/ch31.pdf

13. Alman BA, Krajbich JI, Hubbard S. Proximal femoral focal deficiency: results of rotationplasty and Syme amputation. *J Bone Joint Surg Am*. Dec 1995;77(12):1876-82.

14. Borggreve J. Kniegelenksersatzdurch das in der Beinlangsachse um 180 degree gedrehtefussgelenk.*ArchOrthop*. 1930;28:175-178.

15. Van Nes CP. Rotation-plasty for congenital defects of the femur.Making use of the shortened limb to control the knee joint of a prosthesis. *J Bone Joint Surg*. 1950;32B:12-16.

16. Fowler E, Zernicke R, Setoguchi Y, Oppenheim W. Energy expenditure during walking by children who have proximal femoral focal deficiency. *J Bone Joint Surg Am*. Dec 1996;78(12):1857-62.

17. Malawer MM, Price WM: Gastrocnemius transposition flap in conjunction with limb-sparing surgery for primary bone sarcomas around the knee. PlastReconstrSurg 73:741, 1984

18. Tae Won B. Kim, Richard D. Lackman: Survivorship of Endoprostheses in Bone Tumor Reconstruction. University of Pennsylvania Orthopedic journal.Vol 21, May 2011, pg 69-72.

19. P. S. Unwin, S. R. Cannon, R. J. Grimer, H. B. S. Kemp, R. S. Sneath, P. S. Walker. Aseptic loosening in cemented custom made prosthesis for bone tumours of the lower limbs. J Bone Joint Surg [Br] 1996;78-B:5-13.

20**.** G. J. C. Myers, A. T. Abudu, R. Carter, R. M. Tillman, and R. J. Grimer.The long-term results of endoprosthetic replacement of the proximal tibia for bone tumours.Journal of Bone and Joint Surgery - British Volume, Vol 89-B, Issue 12, 1632-1637.

21. Hejna MJ, Gitelis S. Allograft prosthetic composite reconstruction for bone tumors. SemSurgOncol. 1997;13: 18–24.

22. Edmund W. Ek, Warren M. Rozen, Eugene T. Ek, Hannes A. Rudiger. Surgical options for reconstruction of the extensor mechanism of the knee after limb-sparing sarcoma surgery. Arch Orthop Trauma Surg (2011) 131:487–495

23 Horowitz SM, Lane JM, Otis JC, Healey JH (1991) Prosthetic arthroplasty of the knee after resection of a sarcoma of the proximal end of the tibia: a report of sixteen cases. J Bone Joint Surg 73A:286–293

24 Boris Michael Holzapfel, Hans Rechl, Stefan Lehner, HakanPilge, Hans Gollwitzer,and Erwin Steinhauser. Alloplastic Reconstruction of the Extensor Mechanism after Resection of Tibial Sarcoma.Sarcoma Volume 2011, Article ID 545104, 8 pages.

25. Jacob Bickels, MD, James C. Wittig, MD, Yehuda Kollender, MD,Robert S. Neff, BA, Kristen Kellar-Graney, BA, Isaac Meller, MD,and Martin M. Malawer, MD. Reconstruction of the Extensor Mechanism AfterProximal Tibia Endoprosthetic Replacement. The Journal of Arthroplasty Vol. 16 No. 7 2001.

26. Gosheger G, Hillmann A, Lindner N, Rödl R, HoVmann C, Bürger H, Winkelmann W (2001) Soft tissue reconstruction of megaprostheses using a trevira tube. ClinOrthopRelat Res 393(1):264–271

27. Dominkus M, Sabeti M, Toma C, Abdolvahab F, Trieb K, Kotz RI (2006) Reconstructing the extensor apparatus with a new polyester ligament. ClinOrthopRelat Res 453(1):328–334

28. Malawer MM, Price WM (1984) Gastrocnemius transposition flap in conjunction with limb-sparing surgery for primary bone sarcomas around the knee. PlastReconstrSurg 73:741–750

29. Edge SB, Byrd DR, Compton CC, et al. AJCC cancer staging manual, 7th ed. Newyork: Springer, 2010.

30. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumours of the musculoskeletal system.ClinOrthop 1993;286:241-6.

31. E Vidhubala, Latha, R Ravikannan, CS Mani, R Muthuvel, V Surendren, FU John Paul**.** Validation of Cancer Institute Quality of Life Questionnaire Version II for cancer patients in India. Indian Journal of Cancer Vol:48, Issue:4, Page 500-506

32. Stefan S. Bielacket. al, Prognostic Factors in High-Grade Osteosarcoma of theExtremities or Trunk: An Analysis of 1,702 PatientsTreated on Neoadjuvant Cooperative Osteosarcoma StudyGroup Protocols. Journal of Clinical Oncology, Vol 20, No 3 (February 1), 2002: pp 776-790.

33. Bacci G, Ferrari S, Bertoni F, Ruggieri P, Picci P, LonghliA et al. Long term outcome for patients with nonmetastatic osteosarcoma of the extremity treated at the InstitutoOrthopedico Rizzoli according to the InstitutoOrthopedico Rizzoli/ Osteosarcoma -2 protocal: an updated report. J ClinOncol 2000; 18:4016-27

34. A. SérgioPetrilli et al. Results of the Brazilian Osteosarcoma Treatment Group Studies III and IV: Prognostic Factors and Impact on Survival. J ClinOncoVol 24; Number 7. March 2006.

35. Spanier SS, Shuster JJ, Vander Griend RA. The effect of local extent of the tumor on prognosis in osteosarcoma.J Bone Joint Surg Am. 1990 Jun;72(5):643-53.

36. Allen M. Goorin et al. Presurgical Chemotherapy Compared With Immediate Surgery

andAdjuvant Chemotherapy for NonmetastaticOsteosarcoma:Pediatric Oncology Group Study POG-8651. Journal of Clinical Oncology, Vol 21, No 8 (April 15), 2003: pp 1574-1580

37. Huvos AG, Rosen G, Marcove RC. Primary osteogenic sarcoma: pathologic aspects in 20 patients after treatment with chemotherapy en bloc resection, and prosthetic bone eplacement. Arch Pathol Lab Med 1977;101(1):14.

38. Salzer-Kuntschik M, Delling G, Beron G, et al. Morphological grades of regression in osteosarcoma after polychemotherapyâ€”study COSS 80. J Cancer Res ClinOncol 1983; 106(Suppl):21.

39. Picci P, Bacci G, Campanacci M, et al. Histologic evaluation of necrosis in osteosarcoma induced by chemotherapy. Regional mapping of viable and nonviable tumor.Cancer 1985;56(7):1515.

40. SigbjornSmeland et al. Scandinavian experience in classical osteosarcoma, results of the SSG XIV protocol. ActaOrthopaedica (Suppl 334) 2009;80.

41. P. Picci et al. Risk factors for local recurrences after limb-salvage surgery for high-grade osteosarcoma of the extremities. Annals of Oncology 8: 899-903, 1997.

42. D. Andreouet al. The influence of tumor- and treatment-related factors on the development of local recurrence in osteosarcoma after adequate surgery. An analysis of 1355 patients treated on neoadjuvant Cooperative Osteosarcoma Study Group protocols. Annals of OncologyVolume22, Issue5Pp. 1228-1235.

43. Torbert, Jesse T MD et al. Endoprosthetic Reconstructions: Results of Long-term Followup of 139 Patients. Clinical Orthopaedics & Related Research: September 2005 - Volume 438 - Issue - pp 51-59

44. Bacci G et al. Predictive factors for local recurrence inosteosarcoma. ActaOrthopScand 1998; 69 (3): 230-236

45. MayilVahananNatarajan, A. Sivaseelam, G. Rajkumar and S. H. JaheerHussain. Custom megaprosthetic replacement for proximal tibial tumours.International Orthopedics, Volume 27, Number 6, 334-337

46. Adam J. Schwartz MD, J. Michael Kabo PhD,Fritz C. Eilber MD, Frederick R. Eilber MD,Jeffrey J. Eckardt MD. Cemented Endoprosthetic Reconstruction of the Proximal Tibia.ClinOrthopRelat Res (2010) 468:2875–2884.

47. Flint MN, Griffin AM, Bell RS, Ferguson PC, Wunder JS.Aseptic loosening is uncommon with uncemented proximal tibiatumor prostheses. ClinOrthopRelat Res. 2006;450:52–59

48. Wu CC, Henshaw RM, Pritsch T, Squires MH, Malawer MM.Implant design and resection length affect cemented endoprosthesissurvival in proximal tibial reconstruction. J Arthroplasty.2008;23:886–893

49. Vijay Titus MS (Orth), Dip Orth, Mark Clayer MD, MBBS, FRACS, FAOrthA. Protecting a Patellar Ligament Reconstruction after ProximalTibial Resection.ClinOrthopRelat Res (2008) 466:1749–1754

50. Zhang Y, Yang Z, Li X, Chen Y, Zhang S, Du M, Li J**.** Custom prosthetic reconstruction for proximal tibial osteosarcoma with proximal tibiofibular joint involved. SurgOncol. 2008 Aug;17(2):87-95

51. Shimose S, Sugita T, Kubo T, Matsuo T, Ochi M. Reconstructed patellar tendon length after proximal tibia prosthetic replacement. ClinOrthopRelat Res. 2005;439:176–180

ABSTRACT

Limb salvage surgery in osteosarcomas of the upper end of the tibia encompasses several challenges. Among those challenges lack of soft tissue cover, higher rates of prosthesis failure and difficulty in reconstructing extensor mechanism of the knee joint are important.

Retrospective analysis of 41 consecutive patients undergoing limb salvage surgery for proximal tibialosteosarcomas at our institute from 2001 to 2011.16 patients underwent reconstruction with endoprosthesis and myoplasty (gastrocnemius muscle flap) and 25 patients underwent reconstruction with mesh-myoplasty (using prolene mesh for reconstruction of the extensor mechanism). The 5 yr overall survival and disease free survival was 85.5% and 70.6%. Patients who has 3 to 4 cycles of preoperative chemotherapy had significantly better 5 year overall survival then those who received 5 to 6 cycles of chemotherapy. (94.1% versus 68.6%). 9 patients (22%) had tumour necrosis >90% and 32 patients (78%) had tumour necrosis =<90%, but there was no statistically significant difference in the overall survivals of these two groups (87.5% versus 84.6%). The mean prosthesis survival was 34.5 months (range 2.3 months to 133.1 months). The 5 year prosthesis survival was 86.5%. Infection (3), aseptic loosening (3) and fracture of the prosthesis (2) were the main reasons for prosthesis failure. There was no statistically significant difference in the prosthesis survival between the cases that underwent myoplasty and meshmyoplasty.

Quality of life analysis was done using the Cancer Institute QOL questionnaire II and functional outcomes were evaluated with MSTS scoring system (mean score 74.5%). There was no statistically significant difference in the quality of life outcomes or functional outcomes according to these scoring systems. But the mean extensor lag in the patients undergoing myoplasty was 68.13^0 and the mean extensor lag in the patients undergoing mesh-myoplasty was 36.66^0 and the difference was statistically significant (p=0.004). 2 patients with meshmyoplasty had 0^0 extensor lag whereas none of the patients with myoplasty had 0^0 extensor lag.

8 patients had lung metastasis, 1 patient had local recurrence and 1 patient had both local recurrence and lung metastasis.

The prosthesis survival and the functional outcomes (MSTS scores) in our series is comparable to the other series in literature on endoprosthetic reconstruction for proximal tibial osteosarcomas.

Keywords: Custom made endoprosthesis, proximal tibial osteosarcoma, limb salvage surgery

AIMS OF THE STUDY

1. TO STUDY THE SURVIVAL OUTCOMES OF THE PATIENTS UNDERGOING LIMB SALVAGE SURGERY IN PROXIMAL TIBIAL TUMOURS WITH CUSTOM MADE MEGAPROSTHESIS.

2. TO COMPARE THE QUALITY OF LIFE ASSESSMENT BETWEEN GROUPS UNDERGOING EXTENSOR MECHANISM RECONSTRUCTION WITH OR WITHOUT A PROLENE MESH.

3. TO STUDY THE EARLY AND LATE COMPLICATIONS.

4. TO STUDY THE PROSTHESIS SURVIVAL TIME AND THE FACTORS AFFECTING PROSTHESIS SURVIVAL.

INTRODUCTION

"Walking is man's best* medicine"** ***- Hippocrates

Bony sarcomas arising from the proximal end of the tibia constitute the second most common site of occurrenceafter the distal end of the femur. However this area is a difficult site to perform a safe limb sparing resection in which function is preserved due to anatomical constraints and also surgical technique. Historically amputation had been the treatment for bony sarcomas. The use of effective chemotherapeutic regimen, modern imaging technology and advances in surgical techniques has broadened the horizon and scope of limb salvage surgery in this site. The primary difficulty in doing a limb salvage surgery for sarcoma of the proximal tibia is due to the local anatomy. A difficult surgical approach, intimate relationship to the neurovascular structures, inadequate soft tissue coverage are few of the challenges surgeons face during procedures at this site. Another important factor is the need to reconstruct the extensor mechanism of the knee joint. Many surgical techniques and reconstruction mechanisms have been described for the tumours at this site and have provided satisfactory survival and functional outcomes.

REVIEW OF LITERATURE

HISTORY OF BONE SARCOMAS

Osteosarcoma as a disease was recognised since ancient times. An English surgeon named John Abernathy coined the term "sarcoma" in 1804 which was derived from Greek roots and means "fleshy excrescence."[1] Alexis Boyer a French surgeon (personal surgeon to Napoleon) recognised that sarcomas arising in the bone are a distinct entity from other bony lesion and is credited with using the term osteosarcomas for the first time in 1805.[1]

The gross pathological appearance of this tumour was accurately described by Guillaume Dupuytren in 1847. He the described the appearance as the following:

"Osteosarcoma, which is a true cancerous degeneration of bone, manifests itself in the form of a white or reddish mass, lardaceous and firm at an early stage of the disease; but presenting at a later period, points of softening, cerebriform matter, extravasating blood, and white or straw coloured fluid of a viscid consistence in its interior."[1]

As there was limited experience to guide the surgeons of that time a Registry of Bone Sarcoma was created in 1921 under the auspices of the American College of Surgeons, by Ernest Amory Codman (along with James Ewing and Joseph Bloodgood).[2]

Great advances were made in the field of pathology of bone tumours in the mid-1900s. Henry Jaffe and Louis Lichtenstein published textbooks on bone pathology that established many of the important pathological criteria which are used to diagnose the commonly seen bone tumours.

Dr Norman Jaffe and few others popularised the use of chemotherapeutic drugs for osteosarcomas in the 1970s and early 1980s.[3] Most commonly Adriamycin and methotrexate were used. At MSKCC Rosen found out that these chemotherapeutic drugs useful both

preoperatively as well as postoperatively while studying the patients who were awaiting the custom made prosthesis for their surgery.[4]

William F. Enneking is an eminent name in the field of orthopaedic oncology. He introduced the a surgical staging system for bone sarcomas and trained many orthopaedic oncology fellows, several research papers have been published by him and actively conducted continuing medical education course on bone tumours.

The staging system described by Enneking et al is based on GTM: grade(G), location(T), lymph node involvement and metastasis (M). The staging system is as follows:

Stage IA (G1 T1 M0): Low grade intra-compartmental lesion, without metastasis.

Stage IB (G1 T2 M0): Low grade extra-compartmental lesion, without metastasis.

Stage IIA (G2 T1 M0): High grade intra-compartmental lesion, without metastasis.

Stage IIB (G2 T2 M0): High grade extra-compartmental lesion, without metastasis.

Stage IIIA (G1 or G2 T1 M1): Any grade intra-compartmental lesion with regional nodal or distant metastasis.

Stage IIIB (G1 or G2 T2 M1): Any grade extra-compartmental lesion with metastasis.

HISTORY OF LIMB SALVAGE SURGERY AND CUSTOM MADE PROSTHESIS

Amputation was the traditional treatment for osteosarcomsEiselberg in 1897 and Klapp in 1900 are probably the first people to perform limb salvage surgery and used bone grafts to reconstruct the defects. Lexter introduced the concept of using allografts in tumour surgeries. The concept of resection arthrodesis was introduced by Phemister for lesions above the knee and this technique was further refined by Merle D' Aubigne and Dejouany.

Till the 1960s the limb salvage surgery for bone tumours was restricted to benign and lower grade tumours. The development of newer reconstructive techniques including internal fixation led to the cautious use of limb salvage surgeries in high grade sarcomas.[6]

In the 1970s the improvements in imaging techniques (CT scans) and use of effective chemotherapeutic agents led to great advances in the limb salvage surgeries. Musculoskeletal Tumour Society (MSTS) was formed in this decade and met for the first time in 1979.[6]

In the 1980s there were tremendous advances in orthopaedic oncology. Surgical staging system was developed, surgical margins were defined and International Society on Limb Salvage (ISOLS) was formed in 1981. In the ISOLS meet in 1981 they reported a local recurrence rate of 18% and reconstructive failures in 15% and the second symposium held in 1983 in Vienna reported a local recurrence of 11% and reconstructive failures in 10%. The third meet held at Orlando reported a further declinein local recurrence (7%) and reconstructive failures (5%).[6]

PROXIMAL TIBIAL OSTEOSARCOMAS

The most common site of primary bone tumours is distal end of the femur and the proximal end of the tibia is the second most common site. 12% to 15% of osteosarcomas, 11% of Ewing's sarcoma and 6% of chondrosarcomas are located at the proximal end of the tibia.[7,8]The treatment for the proximal tibial tumours was routine amputation before the 1970s. Cades in 1955 followed a regimen of local radiotherapy and followed by amputation only if there was no evidence of distant spread within 6 months, however the outlook remained poor.[9]

Over the past 25 years the concept of limb salvage surgery has grown dramatically. Adriamycin- and methotrexate based chemotherapy which was introduced in the 1970s at Memorial–Sloan Kettering, New York University, and the Children's Hospital of Philadelphia made a huge impact in the prognosis and management of patients with bone sarcomas. Pioneering work by surgeons such as Ralph Marcove, Kenneth Francis, andHugh Watts led to the development of the techniques of limb salvage surgery.

Nowadays 90–95% of patients with extremitysarcomas who are being treated at centres specializingin musculoskeletal oncology are undergoing limb salvage surgery successfully. Advances in several fields have brought about this dramatic change. The following advances are the important ones among them.

1. Tumour biology and natural history are better understood.
2. There exists an effective induction chemotherapy with which even borderline cases can be salvaged.
3. Advancements in surgical techniques have brought about better functional outcomes. Even limbs in which the vessels have been involved can be salvaged with vascular grafts.
4. Better appreciation of biomechanics of the musculoskeletal system has led to better designing of the prosthesis and better outcomes functionally.

5. Novel materials are being used in the manufacturing of prosthesis due to advances in material engineering.

6. Prosthesis has been developed for virtually every site in the extremity which has been affected by bony tumours.[10]

However when considering a limb salvage surgery instead of an amputation certain factors have to be kept in mind

1) There should not be an increased risk to the patient's life because of the procedure.

2) Functional result should be better.

3) Complication rate must be acceptably low.

4) Patient and attenders must be fully informed about the procedure, the complications and the rehabilitation process.[9]

Several technical issues have to be addressed for the successful outcome of a limb salvage surgery.

a. Key neurovascular structures must be identified and preserved.
b. Oncological safe margins must be obtained, and preservation of a limb must never take priority over thesurvival of the patient. Meticulous surgical technique is necessary for achieving a safe margin
c. Reconstruction of the axial skeleton must be done with appropriate prosthesis
d. Restoration of good soft-tissue cover isnecessary for good prosthesis function and life.[10]

Patient selection for limb salvage surgeries

The introduction of effective chemotherapeutic agents for osteosarcoma has expanded the scope of limb salvage surgery. But the increased survival rates have now placed greater

importance on the functional outcome and the prosthesis survival. Today reconstruction has to take into account the functional, cosmetic and also the psychological needs of the patient.[10]

The most important factors that decide about decision to perform a limb salvage surgery successfully are location of the tumour and the involvement of neurovascular structures.

Picci et al. listed 6 anatomical sites where providing sufficient margins for resection is a problem.[11]

1. Popliteal space.
2. Joint structures.
3. Medullary canal.
4. Soft tissue involvement.
5. Venous thrombi.
6. Sites of periosteal reaction.

However with the use of preoperative chemotherapy many patients who are borderline candidates for limb salvage surgery upfront may ultimately become candidates for limb salvage surgery. The patient should always be re-evaluated after the completionof the chemotherapy and only then the final decision to proceed or not to proceed with the limb salvage surgery must be taken.

The proximal tibial bony sarcomas are a challenging group of tumours in the perspective of limb salvage. Surgical approach to these tumours is difficult, anatomical constraints and inadequate soft tissue cover make providing adequate margins and reconstruction at this site challenging. Providing a good functional outcome with reconstruction of the extensor mechanism is an important aspect of the reconstruction and rehabilitation of this subgroup of patient.

ANATOMICAL CONSIDERATIONS IN THE PROXIMAL TIBIAL SARCOMAS[12]

A. Popliteal artery trifurcation.

Thepopliteal trifurcation is actually a combination of two successive bifurcations. First the anterior tibial arises from the popliteal artery at the lower border of the popliteus.The popliteal artery continues as the tibioperoneal trunk and then bifurcates into peroneal artery and the posterior tibial artery. It may be necessary to ligate the anterior tibial artery to provide adequate soft tissue clearance. The popliteus muscle on the posterior surface of the tibia provides a barrier to the posterior soft tissue extension from the tibia and protects the popliteal artery and its branches.[12]

B. Tibiofibular joint.

Tumours of the proximal tibia have a high incidence of involvement of the tissues of the proximal tibiofibular joint. An en-bloc resection of this joint is usually necessary to provide adequate margin, especially for high grade sarcomas.[12]

C. Knee joint.

The knee joint is not usually directly involved by the tumours of the proximal tibia. This can occur if there has been a fracture or contamination due to a ill performed biopsy procedure. Hemarthrosis suggests intra-articular extension of the disease. MRI of the knee joint provides the most accurate assessment of the knee joint involvement. If knee joint involvement is suspected an extra-articular resection has to be planned.[12]

D. Extensor mechanism.

The reconstruction of the extensor mechanism by reattaching the patellar tendon is a challenging aspect of limb salvage surgery of the proximal tibia. Reconstruction of this

mechanism is necessary for a good function of the lower limb. Various mechanisms of reconstruction of the extensor mechanisms have been tried over the years and these will be described later.[12]

E. Subcutaneous location and less soft tissue coverage.

The medial aspect of the entire length of the tibia occupies the subcutaneous location. This leaves the reconstructed prosthesis in a subcutaneous location and is an important source of infection and prosthesis failure. The use of the medial gastrocnemius muscle has led to provision of adequate soft tissue cover for reconstruction and reduced the incidence of infection, flap necrosis, and secondary infection.[12]The musculotendinous insertion of the medial gastrocnemius was divided and it was rotated to cover the prosthesis and the reconstructed extensor mechanism and sutured to the underlying patellar tendon and the quadriceps muscle.[17]

Various options exist for the reconstruction of these tumours

1. Resection arthrodesis.

Prior to the 1970s this was the main method of reconstruction. It had the advantages of providing good stability, and a durable reconstruction. But as there was no movement at the reconstructed limb as the knee joint was resected and as the result the quality of life was poor. Nowadays due to adequate preservation of soft tissue as a result of effective chemotherapy and use of medial gastrocnemius for soft tissue cover this method is rarely followed.[10]

Fig 1. Intraoperative photograph of resection arthrodesis using dual fibular reconstruction with an intramedullary rod fixation following resection of the distal femur, a technique popularized by Dr William F. Enneking during 1970s.[10]

2. Van Nesrotationoplasty.

This procedure was first described by Borggreve in 1930, but later Van Nes popularized it. Here the lower limb is rotated by 180^0 by knee arthrodesis after resection of the tumour, such that at skeletal maturity the ankle joint of the short limb should be at the level of the contralateral limb knee joint. The foot acts like the residual tibia in a below knee amputation. The functional outcome of Van Nesrotationoplasty is significanty better and also needs less energy expenditure compared to the use of an above knee prosthesis.

Some disadvantages with this procedure are the failure to achieve sufficient rotation during the procedure, subsequent derotation due to continued growth of the skeleton and the unattractive appearance of the leg in which a reversed foot is used. However there are several reports of good patient acceptance and functional outcomes and also acceptable cosmetic acceptance by the patients, prosthetists and surgeons.[13,14,15,16]

3. Allograft reconstruction.

In the 1970s the allograft reconstruction was introduced as a biological solution to the problem of restoring a segmental defect of the skeleton. There have been significant advances in the techniques of fixation of these prostheses and also in the methods of processing the graft so as to preserve the articular cartilage and to lessen the contamination. In spite of these advances the use of allografts is not very popular due to the high rates of complication and prosthesis failure and also due to the stringent means needed to store these grafts. These grafts are procured according to the established guidelines and stored in a fresh frozen state at -80^0C. Even though the allografts are immunogenic the immune response is reduced by the non-vascularity of the graft and also due to the freezing which reduces the antigenicity. The osteoarticular allografts have certain advantages compared to the metallic endoprosthesis. They provide articular surface for the adjacent bone and obviate the need for resection of the articular surface and the growth plate. They also provide ligaments for joint reconstruction and including cruciate ligaments and sites for host tendon reconstruction and provides better functional outcome than the metallic endoprosthesis. However these advantages are offset by significant complications.Early complications are infection,non-union and joint instability, and late complications are instability and allograft fracture.The overall complication rate is more than 50%,which includes an infection rate of 30%. As a reason this is being done at few centres nowadays. This a good option in young patients who are expected to grow and develop substantial limb length discrepancies.

Fig 2. Allograft reconstruction of a proximal tibial tumour.[18]

4. Metallic endoprosthetic reconstruction.

Reconstruction of the proximal tibial tumours by endoprosthesis has been a highly successful procedure. They are either custom made prosthesis or else modular prosthesis. They are made of different alloys, but currently titanium alloy is the preferred one. The custom made prosthesis is relatively less expensive than the modular ones. The modular ones have the advantage of deciding on table for reconstruction depending upon the amount of bone resected. Whereas the custom made prosthesis are prefabricated and is subject to the variations in the tumour size and extent changes during therapy. Bone cement that is polymethlymethacrylate is usually used to fix this prosthesis. A press-fit porous stem can also be used instead of using bone cement. In a retrospective study of 1001 custom made prosthesis (which included 493 distal

femoral, 263 proximal femoral and 245 proximal tibial prostheses) aseptic loosening was shown to be the principal mode of failure of the implants.[19] Use of cemented stem allows instant fixation which will allow early rehabilitation and mobilization.

Improvements in the prosthesis design have also led to the improvements in prosthesis survival. In a study by Myers comparing the fixed hinge prosthesis and the rotating hinge prosthesis they found risk of revision for any reason in the fixed-hinge group was 32% at five years, 61% at ten years and 75% at 15 and 20 years, and in the rotating-hinge group 12% at five years, 25% at 10 years and 30% at 15 years. The cemented, rotating hinge design currently offers the best chance of long-term survival of the prosthesis.[20]

Expandable prosthesis is a novel innovation which is very helpful in for replacement in skeletally immature patients. In most of the commonly used expanding prosthesis a surgical procedure is usually required for the subsequent expansions. A novel type of expanding prosthesis called the Stanmore expandable prosthesis (Stanmore Implants, Stanmore Middlesex, United Kingdom) uses a noninvasive technique for the prosthesis expansion. When the patient with the expandable prosthesis is placed at the centre of a rotating electromagnetic field the poles of the magnet within expandable segment of the prosthesis are captured, causing it to rotate. The external field rotates slowly at a fixed speed causing the implant to expand at a rate of 0.23mm per minute (1mm every 4min).

5. Allograft prosthetic composite.

This prosthesis is a transitional step in between the allografts and the metallic endoprosthesis. This was introduced when they found out that the complication rates of the allografts are significantly high. They provide the advantages of biological reconstruction leading to better functional outcomes and also provide the advantage of immediate stability

of the endoprosthesis. However results have shown that this prosthesis also carries the high complication rates associated with the allografts. [21]

TECHNIQUES FOR REPAIR OF THE EXTENSOR MECHANISM

Various techniques have been described in the literature for reconstruction of the extensor mechanism at the knee joint. The degree of surgical resection and also the type of prosthesis used for reconstruction influence the choice of extensor mechanism reconstruction. No randomised trials exist to compare the various methods of extensor mechanism reconstruction. The reconstruction options available according to the prosthesis used are described briefly below.

A. Classic endoprosthesis

Endoprosthesis are a popular means of reconstruction. The main problem with the use of the endoprosthesis is the need to attach the patellar tendon to the metal prosthesis. Various techniques have been described to overcome this problem.[22]

(a) Direct Fixation: Horowitz et al[23] presented a series of 16 patients and in 10 patients the reconstruction of the extensor mechanism was done by coronally splitting the patella and quadriceps tendon and the remnant patella was directly attached to a porous area on the anterior surface of the prosthesis. Functional assessment of 6 of these patients revealed an extensor lag of less than 20^{0} in 4 of these patients. However the direct fixation is associated with a high rate of complications and the 8 year follow up of this series revealed that 60% of these patients had revision or amputation as a result of the complications.

(b) Synthetic soft tissue augments: Many studies have reported the use of textile implants such as Dacron tapes, Trevira tube to fix the patellar ligament remnant to the prosthesis. [24, 25]

The Trevira tube was introduced for extensor mechanism reconstruction by Goshegeret al.[26] 'Ligament Advancement Reinforcement System (LARS®)' which is essentially a polyester ligament used to repair the defect in the patellar ligament and is secured to the prosthesis at the level of tibial tuberosity and also distally at the level of the prosthesis and tibial end interface.[27] Excellent or good functional results were achieved in 59% of the patients but ligament failure was seen in 23% (5 patients).

Fig 3. Modular endoprosthetic system Munich-Luebeck, EskaOrthodynamics GmbH, uebeck, Germany with the tibial fixation device for the double-layered Trevira cord[24]

(c) 'Biological' augmentation with or withoutsynthetic materials

Bickels tried to overcome the lack of healing of the attachment of the extensor apparatus by doing a biological fixation.[25] He used a Dacron® tape to secure the patellar tendon to the prosthesis. He used autologous bone graft to pack the patellar tendon and prosthesis interface and covered it with medial gastrocnemius muscle flap. This provided certain advantages: immediate mechanical fixation, biological reinforcement to the extensor mechanism, and vascularised tissue coverage to minimise infection and facilitate healing.

The biological reinforcement done undergoes osseointegration to the underlying porous-coated surface of the endoprosthesis. At 12 weeks a layered tendon – fibrocartilage – bone interface can be seen which resembles a normal tendon insertion. Quality of repair was also robust with few patients requiring secondary procedures for reinforcement.

Kotz and Coombs[22] reported the use of pedicled fibular graft for attachment of the patellar tendon and reconstruction with an endoprosthesis. This provides an advantage of doing a biological reconstruction without the use of synthetic material. The fibular graft was based on the peroneal vessels and attached to the tibial mid-shaft using screws and its proximal end was attached to the patellar tendon.

B. Allograft–endoprosthesis composites

Though theoretically the composite prosthesis are an attractive option, the high rates of failure of the allograft and subsequent failure of the extensor mechanism is discouraging. This method of reconstruction is also plagued by a high rate of infection. Donato reported an infection rate of 25%.[22]

C. Biologic reconstruction

Allograft allows direct attachment of the tendons and the ligaments to provide good functional outcome. Host patellar tendon is directly attached to the allograft. This can be reinforced with muscle flap to minimise the chances of infection and helps in healing. Excellent functional outcomes have been reported. In a case series of 34 cases of proximal tibial reconstruction using allograft by Ayerzaet al.[22] they found that the reconstructed tendon was stable in all patients at a mean follow up of 52 months. 24 patients had no extensor lag and the remaining 10 had a mean lag of 6.5^{0} . However this technique has a very high

complication rate. Clohisy et al reported that 15 of the 16 allografts for the proximal tibia had complications and 7 required removal.[22]

Muscle Flaps

The muscle flaps provide the soft tissue coverage for the prosthesis. This reduces the risk of infection, facilitates healing and also provides a mechanism for reconstruction of the extensor mechanism. Muscle flaps, in particular the pedicled gastrocnemius flap has been very popular. This was first used by Dubousset et al. This can be usedas a muscle or a myocutaneous unit. He described two techniques. The first one in which the patellar tendon was intact the medial gastrocnemius was transposed anteriorly and sutured to the tendon. Here the muscle is not divided at either the proximal or the distal end. In a situation where the patellar tendon is deficient the medial gastrocnemius was divided at its distal end and swung anteriorly and fixed to the underlying fibula and attached to the patellar tendon.[22]Malawer described a technique in which the medial gastrocnemius was rotated over the defect and sutured to the borders of the anterior muscles providing a soft tissue cover over the prosthesis.[28] Other flaps described are a combination of gastrocnemius flap and the semitendinosus tendon autograft, sartorius, biceps femoris, semitendinosus and latissimusdorsi muscle flap.

MATERIALS AND METHODS

Forty one proximal tibialosteosarcoma patients underwent limbsalvage in cancer institute between 2001 and 2011.The case records of these patients were reviewed and followed up for Quality of life assessment after limb salvage surgery.

EVALUATION

Patients suspected of having bone sarcoma were evaluated with X-ray and MRI of the local affected part. Metastatic work up was done with Chest X-Ray, CT Chest and Tc99 bone scintigraphy. The outside slides and paraffin blocks were procured for patients who had undergone biopsy outside. Jamshidi needle biopsy was done at the institute for patients who didn't have a biopsy done outside.

Tumours are staged according to the 7th edition of the AJCC cancer staging manual[29]

Primary tumour (T)

TX – Primary tumour cannot be assessed

T0 – No evidence of primary tumour

T1- Tumour 8 cm or less in greatest dimension

T2- Tumour more than 8 cm in the greatest dimension

T3- Discontinuous tumours in the primary bone site

Regional lymph nodes (N)

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph nodal metastasis

N1 – Regional lymph nodal metastasis

Distant metastasis (M)

M0 – No distant metastasis

M1a – Lung metastasis

M1b – Metastasis to other distant sites

Histological grade (G)

GX – Grade cannot be assessed

G1 – Well differentiated – low grade

G2 – Moderately differentiated – low grade

G3 – Poorly differentiated

G4 – Undifferentiated

STAGE GROUPING

STAGE	T	N	M	G
IA	T1	N0	M0	G1, G2, GX
IB	T2	N0	M0	G1, G2, GX
	T3	N0	M0	G1, G2, GX
IIA	T1	N0	M0	G3, G4
IIB	T2	N0	M0	G3, G4
III	T3	N0	M0	G3, G4
IVA	Any T	N0	M1a	Any G
IVB	Any T	N1	Any M	Any G
	Any T	Any N	M1b	Any G

NEO-ADJUVANT CHEMOTHERAPY

Neoadjuvant chemotherapy with ifosphamide, adriamycin and cisplatin were given for two cycles and the response to chemotherapy was assessed clinically and if necessary radiological with MRI. If the patient was found to be a candidate for limb salvage then a scanogram of the affected limb was taken and depending on the dimension of the tumour, the bone scan length of the lesion and the dimensions of the remaining bone the custom made prosthesis design was prepared and ordered for fabrication.

Fig 4. Custom made megaprosthesis made of titanium alloy with the grooves for insertion of the prolene mesh

SURGERY

Surgery is usually performed after 3 to 4 cycles of neo-adjuvant chemotherapy, depending on the response to the neo-adjuvant therapy. Repeat imaging is done for reassessment of the borderline resectable tumours. Limb salvage surgery is done with custom made mega-prosthesis.

Surgicalprinciples:

Adhering to the surgical principles of limb salvage and maintaining thorough aseptic precautions at each phase of the surgery isthe key for the successful outcomes and avoiding preventable complications. It includes thorough pre-surgical scrub with antiseptic solution the day before and on the day of surgery and after induction of anaesthesia.

Incision:

Incision is placed on the medial aspect starting at the lower end of the femur and extended across the knee joint to the middle or lower third of the leg. Incision should include the previous biopsy scar. Thick fasciocutaneous flaps are raised

Popliteal vessel dissection :

Early popliteal exploration is the key to assess the resectabilty of the tumor.

Popliteal space and trifurcation of the popliteal artery is exposed by dissection. Care should be taken to preserve the vascular supplyto the medial gastrocnemius which is by the medial sural artery which goes in a posteromedial direction to the geniculate artery. Further vascular dissection is done by and dividing the medial gastrocnemius insertion and splitting the soleus muscle.

Knee joint exposure:

The capsule is incised circumferentially 1 cm away from the tibia and the patellar tendon. The cruciate ligaments are visually exposed and transected and the knee joint is opened.

Peroneal nerve exposure and tibiofibular joint resection:

Lateral fasciocutaneous flap is raised to expose the proximal fibula and the peroneal nerve.The tibio-fibular joint is resected en-bloc along with the tumour.

Bone cuts:

Distally tibia is transected 3 to 4 cm from the bone scan uptake margin and proximally articular plate of femur is transected and the specimen is removed enbloc.

Fixation of prosthesis:

Cut ends of the bone are reamed with reamer to accommodate the prosthesis. Bone cement (PMMC) is used to fix up the tibial prosthesis in position after checking the alignment.

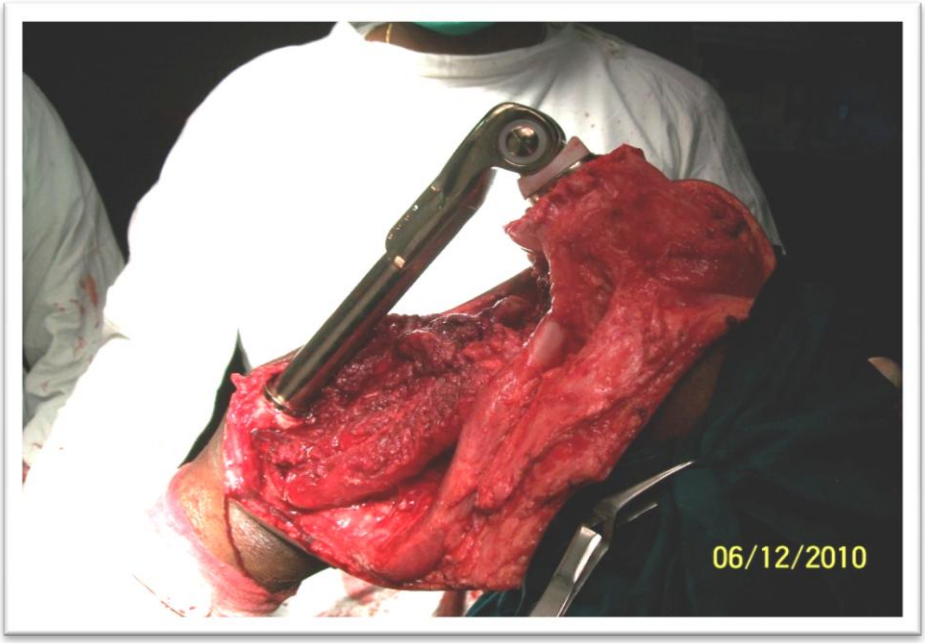


Fig 5. Fixing the prosthesis with bone cement after ensuring correct alignment

Soft tissue and Extensor reconstruction:

Extensor mechanism is reconstructed using prolene mesh anchored to the prosthesis and the patellar ligament using non absorbable suture material prolene. Medial gastrocnemius is mobilized to provide coverage for the prosthesis and mesh and sutured to the muscles in the anterior compartment.

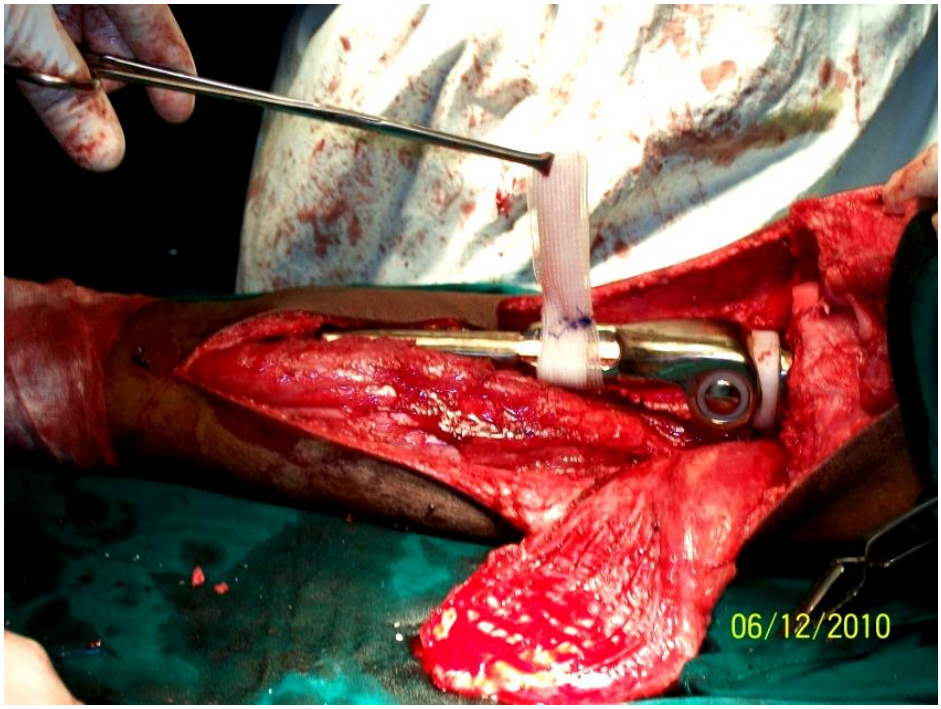


Fig 6. Fixing the prolene mesh to the prosthesis

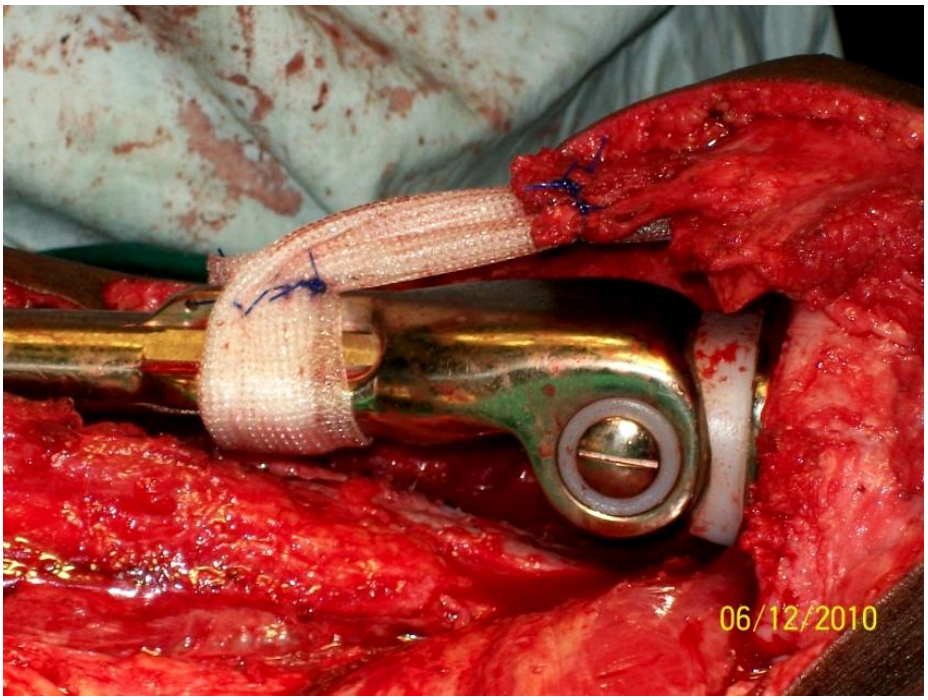


Fig 7. Fixing the prolene mesh to the distal end of the patellar tendon

Fig 8. Medial gastrocnemius muscle flap used to wrap around the prosthesis and the reconstructed extensor mechanism

Wound closure:

After ensuring complete haemostasis, suction drains are placed and majority of the wounds are closed primarily and some cases required skin grafting to achieve closure of the wound.

Rehabilitation

Patient's knee was kept extended to allow the reconstructed extensor mechanism to heal. Static quadriceps exercises are begun on day 7, non-weight bearing mobilization is begun at 2 to 3 weeks, weight bearing mobilization is begun at 4-6 weeks and full weight bearing is begun at 6-8 weeks. All the rehabilitation is done under the supervision by our physiotherapists.

FOLLOW UP

Patients after completion of treatment were followed up according to the institute protocol. Monthly in first year, two monthly in the second year, three monthly in the third year, six monthly in the fourth and fifth year and then annually. Every visit includes clinical examination, chest x-ray, physiotherapy. Quality of life assessment and extensor lag were measured after 6 months of the procedure. Further investigation were done as clinical symptoms and sign warranted.

Extensor lag measurement:

To measure the extensor lag the patient was put in a high sitting posture and using a goniometer the range of movements and the lag in extension from full extension was measured.

Fig 9.Measurement of the extensor lag using a goniometer.

COMPLICATIONS AND ITS MANAGEMENT

Patients after limbsalvage surgery face with varieties of complication and they were managed appropriately. Marginal skin necrosis was managed mostly by conservative treatment rarely

some required debridement and secondary suturing, skin grafting or local flaps. Major complications were approached with redoprosthesis for prosthesis fracture, prosthesis removal or amputation for prosthesis infection, amputation for local recurrence and metastectomy for resectable lung metastasis in a patient with good performance status and adequate disease free survival.

ASSESSMENT OF THE QUALITY OF LIFE AND FUNCTION OUTCOME

Functional outcome assessment was done using the musculoskeletal tumour society scoring system (MSTS)[30] and Quality of life by Cancer Institute Quality of life Questionnaire Version II[31].

Scoring system – International society of limb salvage

SCORE	PAIN	FUNCTION	EMOTIONAL ACCEPTANCE	SUPPORTS	WALKING ABILITY	GAIT
5	None	No Restriction	Enthuse	None	Unlimited	Normal
4	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
3	Moderate	Restriction in recreational activities	Satisfied	Brace	Limited	Minor cosmetic
2	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
1	Moderate	Partial disability	Accepts	One cane or crutch	Household	Major cosmetic, minor handicap
0	Severe	Total disability	Dislikes	Two canes or crutches	Unable to walk unaided	Major cosmetic, minor handicap

Cancer Institute QOL questionnaire[31] consisted of 42 variables and the maximum score was 180. Higher the score better the quality of life. The interpretation of the QOL II version is as follows:

1. <99 – Significantly poor

2. 99-117 – Below average

3. 118-146 – Average

4. 147 – 165 – Above average.

5. >165 – significantly high

STATISTICAL ANALYSIS

Statistical analysis was done by SPSS 17 (SPSS software Inc USA). Extensor lag and quality of life assessment were analysed by T –test.

RESULTS

41 consecutive patients who underwent limb salvage surgery for proximal tibial osteosarcomas from 2001 to 2011 were analysed.

Mean age of the patients was 17.7 years (range 9-35 years). There were 15 patients with age more than 18 years and 26 patients with age up to 18 years.

29 patients (70.7%) of the patients were male and 12 patients (29.3%) were females.

J needle biopsy was used for the diagnosis in 32 patients (78%) and open biopsy was performed in 9 patients (22%). Of note, no open biopsies were performed in our institute. All of the 9 open biopsies were done outside and the slides were reviewed here.

Preoperative biopsy was the follows

Histiology	Frequency
Classical osteosarcoma high grade	19
Chondroblastic osteosarcoma	8
Pleomorphic sarcoma	11
Fibroblastic osterosarcoma	1
Giant cell tumour of bone	1
Chondrosarcoma	1

The average bone scan length was 13.5 cms and 30 patients had bone scan length of up to 15 cms and 11 patients had bone scan length more than 15 cms.

CT chest done upfront showed nodules in the chest in 4 patients. Among these patients 3 had solitary pleural based nodule and 1 patient has 2 nodules. However only one patient among

the three with solitary nodule in the chest developed lung metastases after limb salvage with a DFS of 20.2 months and he underwent metastectomy twice. His overall survival was 70.1 months.

Neoadjuvant chemotherapy was given in all but 2 patients. These two patients had a preoperative diagnosis of giant cell tumour of the bone and chondrosarcoma respectively. 32 patients received either 3 or 4 cycles of neoadjuvant chemotherapy. 7 patients received either 5 or 6 cycles of neoadjuvant chemotherapy.

16 patients underwent reconstruction with endoprosthesis and myoplasty (gastrocnemius muscle flap) and 25 patients underwent reconstruction with mesh-myoplasty (using prolene mesh for reconstruction of the extensor mechanism). 31 patients had resection of the fibular head and 22 patients had ligation of the anterior tibial artery during resection of the tumour. 6 patients needed SSG cover during the procedure.

Early complication

Complications occurring within 30 days of the surgery were considered as early complications.

Early complication	Frequency	Treatment
Foot drop	14	Conservative
Skin necrosis	6	Conservative (2), flap cover (1) and secondary suturing (3)
Foot drop and skin necrosis	1	Conservative

Over all 51.2% patients had early minor complications. However about 50% of them were foot drops which recovered in most of the patients. None of them had any major complication in the early postoperative period for which removal of prosthesis was necessary.

Complications occurring after 30 postoperative days were considered as late complications. Over all 10 patients had late complications (24.4%).

Late complication	Frequency	Treatment
Infection	3	Prosthesis removal (2) Amputation (1)
Fracture prosthesis	2	Redoprosthesis (1) Patient was not willing for redoprosthesis (1)
Aseptic loosening	3	Redoprosthesis (3)
Exposed prosthesis	1	Prosthesis removal
Fracture of the limb proximal to the prosthesis	1	Open reduction and internal fixation

Post-operative histopathology

Histology	Frequency
Classical osteosarcoma	23
Chondroblastic osteosarcoma	9
Pleomorphic sarcoma	1
No residual tumour	7
Giant cell tumour rich osteosarcoma	1

Tumour necrosis:

Percentage of necrosis in the post-operative specimen was examined

Percentage of necrosis	Frequency
$>90^0$	9 (22%)
0^0 to 90^0	32 (78%)

Recurrence:

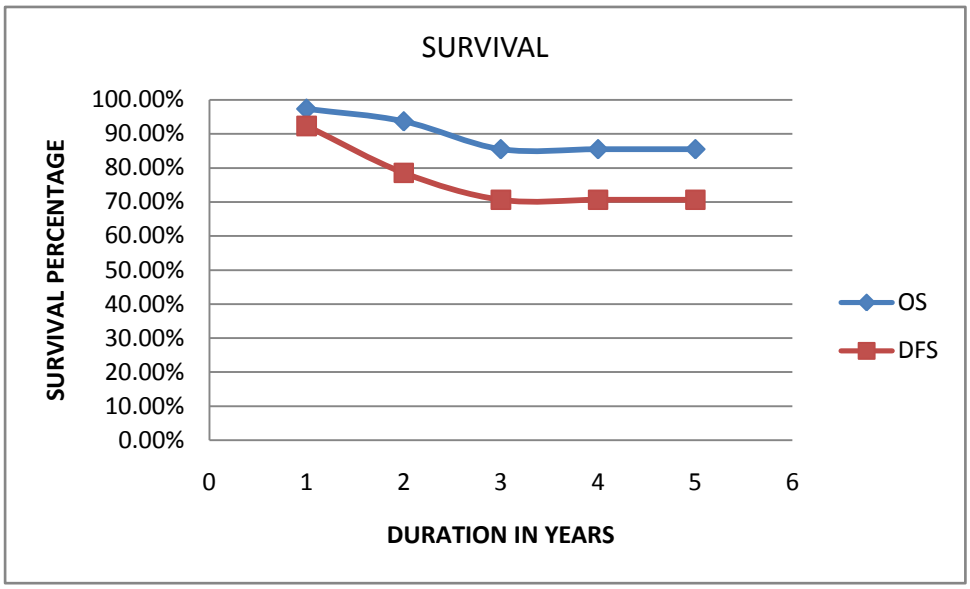
10 patients (24.4%) had recurrence on followup.

Site of recurrence	Frequency
Local	1
Distant	8
Local and distant	1

Overall only 2 patients (4.8%) had local recurrence and 9 patients (21.95%) had lung metastasis. The patient with both local and distant recurrence was offered only supportive care. The patient with only local recurrence defaulted for evaluation. Of the 8 patients with only distant metastasis 6 were offered supportive care (due to multiple bilateral metastasis)and 1 patient underwent metastectomy twice and had chemotherapy. The other patientunderwent metastectomyonce.

Survival analysis was done using SPSS 17.0 version and Kaplan Meyers analysis.

5 years overall survival and disease free survival were 85.5% and 70.6% respectively. In both the overall survival and the disease free survival the events occurred during the first 2 years. The mean overall survival was 38 months and mean disease free survival was 34 months.

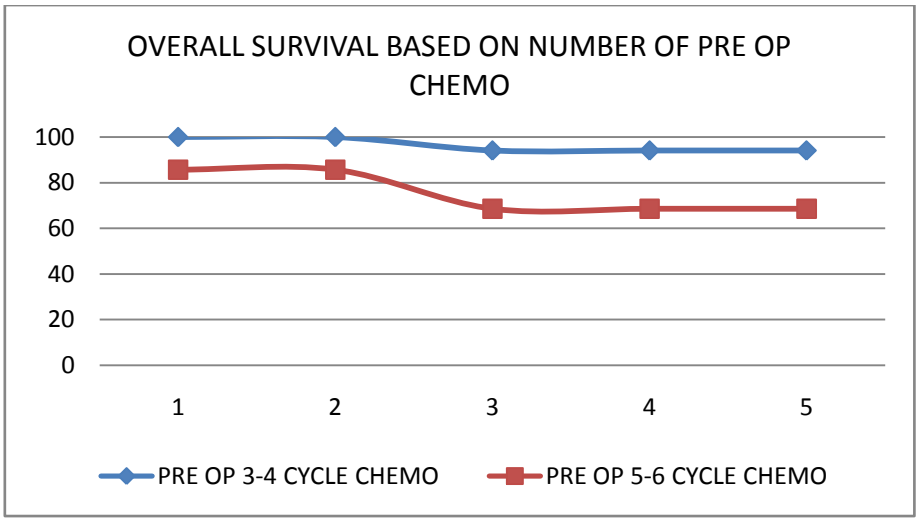


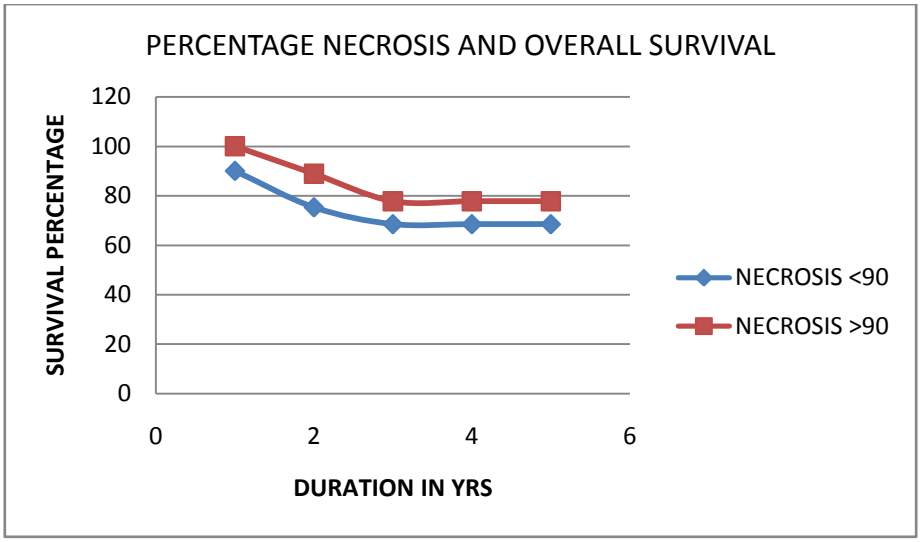
Factors like age of the patient, type of biopsy, bone scan length of the lesion, number of preoperative chemotherapy cycles, type of surgery and amount of necrosis in the post-operative specimen were evaluated for impact on survival.

Among these there was a statistically significant difference in survival only in patients receiving 3 to 4 cycles of neo-adjuvant chemotherapy versus those receiving 5 to 6 cycles of neo-adjuvant chemotherapy with the 5 year overall survival being 94.1% versus 68.6% respectively

(p= 0.045)

S.No	Variable	5 year overall survival in %	p value
1.	Age upto 18 years	81.4	NS
	Age > 18 years	93.3	
2.	Bone scan length upto 15 cms	85.7	NS
	Bone scan length >15 cms	90.9	
3.	J needle biopsy	84.3	NS
	Open biopsy	87.5	
4	3 to 4 cycles pre op chemo	94.1	0.045
	5 to 6 cycles pre op chemo	68.6	
5	Myoplasty	86.7	0.885
	Meshmyoplasty	84.7	
6	Necrosis upto 90%	84.6	NS
	Necrosis >90%	87.5	





Disease free survival:

Similarly these factors were analysed for any influence on the disease free survival.

S.No	Variable	5 year Disease free survival in%	p value
1.	Age upto 18 years	64.8	NS
	Age > 18 years	80	
2.	Bone scan length upto 15 cms	64.3	NS
	Bone scan length >15 cms	90.9	
3.	J needle biopsy	75.5	NS
	Open biopsy	53.3	
4	3 to 4 cycles pre op chemo	76.9	NS
	5 to 6 cycles pre op chemo	53.6	
5	Myoplasty	80.8	NS
	Meshmyoplasty	62	
6	Necrosis upto 90%	68.5	NS
	Necrosis >90%	77.8	

Prosthesis survival:

The mean prosthesis survival was 34.5 months (range 2.3 months to 133.1 months). The 5 year prosthesis survival was 86.5%. All of the prosthesis failures occurred in the first 3 years. Prosthesis survival was analysed with respect to bone scan length, type of surgery (myoplasty versus meshmyoplasty), depending on the type of the biopsy and whether the patient received 3 to 4 or 5 to 6 cycles of pre-operative chemo.

S.No	Variable	5 year prosthesis survival in%	p value
1.	Bone scan length upto 15 cms	89.8	NS
	Bone scan length >15 cms	85.7	
2.	J needle biopsy	88.7	NS
	Open biopsy	77.8	
3.	3 to 4 cycles pre op chemo	89.3	NS
	5 to 6 cycles pre op chemo	71.4	
4	Myoplasty	93.8	NS
	Meshmyoplasty	79.9	

There was no statistically significant difference in the prosthesis survival between the cases that underwent myoplasty and meshmyoplasty.

Quality of life assessment:

Quality of life assessment was done based on the Cancer Institute QOL questionnaire II for cancer patients[31]and the MSTS scoring system[30] was used for the functional outcome.

Of the 41 patients 4 of the patients were lost to follow-up and were not available for QOL assessment. 2 patients died and 2 patients had their prosthesis removed before the time of QOL assessment. So QOL was done for 33 patients and among these 24 had undergone meshmyoplasty and 9 had undergone myoplasty. Following are the results of the analysis.

QOL Variable	Myoplasty	Mesh-myoplasty	p Value using T test
QOL total	148.89	144.17	0.197
General well being	25.78	23.71	0.075
Physical well being	37.11	36.0	0.139
Psychological well being	23.89	24.71	0.627
Interpersonal relationship	15.44	14.63	0.207
Sexual and personal ability	4.78	4.50	0.713
Cognitive well being	11.00	11.21	0.642
Optimism and belief	7.67	7.50	0.599
Economical well being	8.78	8.67	0.875
Information support	7.56	6.46	0.035
Patient physician relationship	4.00	3.88	0.414
Body image	2.89	2.92	0.937

QOL analysis between the two type of surgeries i.e. myoplasty and mesh-myoplasty did not show any statistically significant outcomes in the overall quality of life. However theover all QOL was slightly better in the analysis done for information support. Information support was concerned with the amount of information the patient expected and the amount of information the patients were able to get from the doctors.

Functional outcome was assessed using the MSTS scoring system[30]

A total of 6 factors were analysed and the following are the results.

MSTS variable	Myoplasty (mean)	Mesh-myoplasty (mean)	p Value using T test
PAIN	4.78	4.67	0.599
FUNCTION	3.56	3.33	0.479
EMOTIONAL ACCEPTANCE	2.89	3.50	0.031
SUPPORTS	4.44	4.54	0.748
WALKING ABILITY	3.56	3.29	0.397
GAIT	3.11	3.04	0.805
TOTAL	22.33	22.38	0.964

This shows that the overall functional outcome between the patients undergoing myoplasty and mesh-myoplasty was similar. However when the patients were analysed based on the emotional acceptance of the patients, the patients undergoing mesh-myoplasty showed a statistically better outcome (p=0.031) than the group undergoing myoplasty.

EXTENSOR LAG ANALYSIS

Extensor lag was measured for 32 patients (8 with myoplasty and 24 with meshmyoplasty). 4 patients were lost to follow up, 3 patients were dead and 2 patients had their prosthesis removed due to infection prior to the time when the extensor lag was measured.

The mean extensor lag in the patients undergoing myoplasty was 68.13^0 and the mean extensor lag in the patients undergoing mesh-myoplasty was 36.66^0 and the difference was statistically significant (p=0.004).

Type of surgery	0^0	$1^0 – 20^0$	$21^0 – 50^0$	$51^0 – 70^0$	$>70^0$
Myoplasty	0	0	1	3	4
Mesh-myoplasty	2	5	13	1	3

None of the patients in the myoplasty arm had an extensor lag of less than 21^0 . Whereas 2 patients with mesh-myoplasty had 0^0 extensor lag.

DISCUSSION

The management and the outcomes including the survival and the functional outcomes of proximal tibial osteosarcomas has changed considerably due to the use of chemotherapy, use of advanced imaging technology and refinements of surgical techniques. The prosthesis survival also has increased due to use of better quality and designing of prosthesis. Endoprosthetic reconstruction is now the preferred method used for reconstruction with various methods used for reconstruction of the extensor mechanism which is one of the important factors affecting the functional outcomes.

In our study we included 41 consecutive cases of proximal tibial osteosarcomas who underwent limb salvage surgery at our institute from 2001 to 2011 with a mean follow up of 38 months.

The mean age of the patients was 17.7 years (range 9-35 years). There were 15 patients with age more than 18 years and 26 patients with age up to 18 years. In the German-Austrian-Swiss co-operative study group comparison of the overall survival of the patients with age of the patients <40 years and >=40 years showed statistically significant difference in favour of the group less than 40 yrs of age

Our study did not show any statistically significant difference in the age group =< 18 years and > 18 years.

Generally many studies have shown that proximal tibial osteosarcomas are a favourable sub-site for the sarcomas[19, 32].

The Cooperative German-Austrian-Swiss Osteosarcoma Study Group[32] in their analysis of 1702 cases of osteosarcomas found that the tumours in the proximal tibia had a 5year and 10 year overall survival of 77.5% and 72.0% respectively, whereas the overall survival in the entire group for 5 years and 10 years was 65.3% and 59.8%.

In the Brazilian osteosarcoma treatment group studies III and IV by SérgioPetrilliet al[34], they found that the overall 5 and 10 year survival was 50.1% and 46.7% whereas it was 60.0% and 56.7% respectively for tumours arising in the proximal tibia

However in our study we have included only cases which had small volume tumours with better prognosis and who have undergone limb salvage surgery where as the other studies quoted have included cases with metastasis and also patients who have undergone amputation.

Various studies have shown that the outcomes with larger tumour volumes have been poorer[32, 33]. In our study we used the bone scan length of the tumour to classify them into 2 categories. They were classified as tumour with bone scan length =<15 cms (30 patients – 73.2%) and tumours >15 cms (11 patients – 26.8%). We did not find any statistically significant difference in the survival in these two subgroups.

If patients are having extensive soft tissue component then it is one of the relative contraindications to performing limb salvage surgery. Spanier et al. from the University of Florida have extensively studied the effect of local extent of the tumour on disease free survival and overall survival.[35]

They studied the effect of the local tumour extent on the disease free survival. They included 51 patients with Enneking stage IIB tumours. They classified the tumours into 6 types depending on the local extent of the tumour.

E1 – Tumour only touches the periosteum but does not elevate or penetrate it.

E2 – Tumour touches and elevates the periosteum but does not penetrate it.

E3 – Tumour penetrates into the periosteum but does not penetrate through the periosteum.

E4 – Tumour penetrates through the periosteum with minimum extraperiosteal extension without invasion of another structure (like muscle, tendon or ligament)

E5- Tumour invades one additional structure

E6 – Tumour invades two or more additional structures.[35]

They found that the risk of failure was 5.9 times higher if tumour involed 2 or more surrounding tissues compared to the other subgroups.[35]

Study	Size of the tumour	OS	p Value	DFS	p Value
German-Austrian-Swiss group[32]	< one third	72.1%	<.0001	61.0%	<.0001
	>= one third	58.4%		42.9%	
Bacci et al[33] based on the tumour volume	=<150 ml			65%	NS
	>150 ml			52%	
SérgioPetrilli et al[34] -tumour length	=<12cms	64.5%	<.0001	48.1%	.009
	>12 cms	40.5%		30.4%	
Spanier SS, Shuster JJ, Vander Griend RA[35]	E1 – E5	82.3%		79.8%	
	E6	37.8%		17.6%	
Our study – Bone scan length	=<15cms	85.5%	NS	64.8%	NS
	>15 cms	64.3%		90.9%	

Chemotherapy

The use of chemotherapy has brought about a revolution in the outlook of these previously lethal tumours. The advantages of giving preoperative chemotherapy include:

1. Early initiation of the systemic therapy.

2. Borderline cases for limb salvage can undergo limb salvage surgery following tumour shrinkage after chemotherapy.

3. The response of the tumour to the chemotherapy can be assessed.

4. Provides time for designing and fabrication of the custom made prosthesis.

However the disadvantage is that the chemotherapeutic agent has to act against a large tumour burden.

Pediatric oncology group conducted a randomised control trial POG 8651, to compare the preoperative chemotherapy versus adjuvant chemotherapy. Of the 100 patients 45 underwent preoperative chemotherapy and 55 underwent straight surgery followed by chemotherapy. The 5 years DFS for undergoing immediate surgery and preoperative chemotherapy was 65% and 61 % (p -.8) and the rate of limb salvage for these groups were 55% and 50% respectively. It was concluded that chemotherapy was effective in both the settings[36]. In our study 2 patients did not receive a preoperative chemotherapy because the preoperative diagnosis for these patients was giant cell tumour of the bone in one case and chondrosarcoma in the other case. As the number of cases undergoing immediate surgery was very less statistical analysis couldn't be done.

The response to neo-adjuvant chemotherapy has been an important prognostic factor for the overall and the disease free survivals. Several centres have developed criteria to

evaluate the chemotherapy response. Huvos et al. at MSKCC[37], Salzer-Kuntschik et al.[38] (system used by the COSS study group) and Picci et al [39] at InstitutiOrthopedico Rizzoli independently developed criteria to assess the tumour response to chemotherapy. But as a consensus a tumour response >90% is taken as good response and =<90% is taken as poor response.

Using this criterion the chemotherapy response was assessed in our study and 30 patients (76.92%) were poor responders and 9 (22%) were good responders.

Response to chemotherapy has been reported by various studies and has been a statistically significant predictor of survival[32, 34, 40]. However the update by Bacciet al[33] did not show any statistically significant difference in the outcomes of poor responders to chemotherapy compared to the good responders.

Huvos et al[37]		Salzer-Kuntschik et al.[38]		Picci et al [39]	
IV	No histologic evidence of viable tumor	I	No viable tumor cells	Good response	90%-99% tumor necrosis
III	Only scattered foci of viable tumor cells	II	Single viable tumor cells or cluster <0.5 cm	Fair response	60%-89% tumor necrosis
II	Areas of necrosis due to chemotherapy with areas of viable tumor	III	Viable tumor<10%	Poor response	<60% tumor necrosis
I	Little or no chemotherapy effect	IV	Viable tumor 10% - 50%		
		V	Viable tumor>50%		
		VI	No effect of chemotherapy		

Response to preoperative chemotherapy and survival outcomes

Study	Disease free survival		p value	Overall survival		p value
	Good responders	Poor responders		Good responders	Poor responders	
COSS study[32]	67.6%	38.6%	<.0001	77.8%	73.4%	<.0001
SigbjornSmeland et al[40]	89%	53%	.004			
Bacci G[33]	62%	51%	NS			
Our study	68.5%	77.8%	0.539	87.5%	84.6%	0.521

Even though our study did not reveal a significant difference in the survival of the patients with poor response to preoperative chemotherapy compared to the patients with good response, the survival curves never met and may be with more number of patients or a longer follow up we may be able to appreciate a difference in survival between these subgroups.

We also analysed the survival of the patients who had received 3 to 4 cycles of preoperative chemotherapy versus those receiving 5 to 6 cycles of preoperative chemo. We found that patients receiving 3 to 4 cycles of chemotherapy had a statistically significant better overall survival (94.1% versus 68.6% with p = .045) compared to the patients who received 5 to 6 cycles of chemotherapy.

We also analysed the survival outcomes with respect to type of surgery (myoplasty v/s meshmyoplasty), whether the fibular head was resected or not, whether the anterior tibial artery was ligated or not and also depending on the type of biopsy (J needle biopsy versus open biopsy). The survival outcomes between the above compared subgroups were not different statistically.

Recurrences

There were 10 cases of recurrence in our series. 1 patient had local recurrence, 1 patient had both local recurrence and distant metastasis and 8 patients had lung metastasis. The mean duration for recurrence or metastasis was 14.97 months (range 4.9 to 26.3 months). The local recurrence rate was 4.8% (2 patients) and the distant recurrence rate was 21.95% (9 patients). Most of the published series for limb salvage surgery have documented involved margins, larger size of the tumour, open biopsy, local response to chemotherapy and low volume centres as significant predictors for local recurrence. [41, 42, 43, 44, 40, 34]

In our study none of the patients had margin positivity and as the number of local recurrences was only 2 statistical analyses couldn't be done.

Our local recurrence rates are comparable with the major published series.

Study	Local recurrence rate
P. Picci et al[41]	7%
D. Andreou et al[42]	5.6%
Sigbjorn Smeland[40]	4%
A. Sérgio Petrilli[34]	10%
Torbert, Jesse T MD et al[43]	6.8%
Bacci G et al[44]	6%
R. J. Grimer, et al.[9]	12.6%
Our study	4.8%

Prosthesis survival

The mean prosthesis survival was 34.5 months (range 2.3 months to 133.1 months). The 5 yr prosthesis survival was 86.5%. All of the prosthesis failures occurred in the first 3 years. Prosthesis survival was analysed with respect to bone scan length, type of surgery (myoplasty versus meshmyoplasty), depending on the type of the biopsy and whether the patient received 3 to 4 or 5 to 6 cycles of pre-operative chemo. There was no statistically significant difference in the above compare subgroups.

Our prosthesis survival of 86.5% is comparable to the various studies quoted in the literature regarding the prosthesis survival.

Study	Proximal tibial Prosthesis survival	
	5 years	10 years
MayilVahananNatarajan et al.[45]	85.5	
Adam J. Schwartz MD et al.[46]	93.8%	86.5%
G. J. C. Myers[20] (fixed hinge)	68%	39%
G. J. C. Myers[20] (rotating hinge)	88%	75%
Flint et al.[47] (fixed hinge)	73%	
Wu et al[48] (custom prosthesis)	44.4%	22.2%
Wu et al[48] (modular prosthesis)	81.4%	65.3%
Our study (over all)	86.5%	
Our study (myoplasty)	93.5%	
Our study (meshmyoplasty)	79.9%	

Even though the 5 yr prosthesis survival was better in the myoplasty arm it did not reach statistical significance. The 8 year prosthesis survival was 64.3% for the myoplasty arm and 79.9% for the meshmyoplasty arm. Most of the events have occurred in the first 3 years. However we need a longer follow up with the meshmyoplasty arm to clearly tell us about the long term outcomes.

Complications

Early complications were taken as the complications occuring within 30 days of the surgery. Of the 41 patients 14 patients had a temporary foot drop which recovery in all but 2 of the patients on followup. 6 patients has mariginal skin necrosis which was managed conservatively in 2, by flap cover in 1 and with secondary suturing in 3 patients. 1 patient had both foot drop and marginal skin necrosis and was managed conservatively

Late complications were taken as those occuring after 30 days of the surgery. In our series 10 patients (24.4%) had late complications. The following were the complication breakdown and the treatment given for them.

Late complication	Frequency	Treatment
Infection	3 (7.31%)	Prosthesis removal (2) Amputation (1)
Fracture prosthesis	2 (4.87%)	Redoprosthesis (1) Conservative treatment(1)
Aseptic loosening	3 (7.31%)	Redoprosthesis (3)
Exposed prosthesis	1 (2.43%)	Prosthesis removal
Fracture of the limb proximal to the prosthesis	1 (2.43%)	Open reduction and internal fixation

In most of the series reported on proximal tibial prosthesis, infection and aseptic loosening has been stated as most common causes for prostesis failure.

Here we compare the infection rates, asceptic loosening rates and prosthesis loosening rates of our study with the other studies stated in literature.

Study		Infection	Asceptic loosening	Fracture prosthesis
Our study		7.31%	7.31%	4.87%
R. J. Grimer, et al.[9]	With gastrocnemius	12%	-	3.31% (5/151)
	Without gastrocnemius	36%		
P. S. Unwin et al.[19]		36.58%	19.51%	4%
Jacob Bickels et al[25]		3.6%	-	3.63%
Myers et al[20]	Fixed hinge	19.5%	46%	1.92%
	Rotating hinge		3%	
Flint MN et al[47]	Uncemented prosthesis	15.9%	0%	4.54%
Adam J. Schwartz et a.l[46]		5.8%	11.53%	
MayilVahananNatarajan et al.[45]		12%		
Wu CC et al.[48]		15.9%		
Horowitz et al.[23]		37.5%		

The major complications in the proximal tibial prosthesis are infection, aseptic loosening and fracture of the prosthesis stem. Infections rates have come down with the use of adequate soft tissue cover, basically used is the medial gastrocnemius muscle flap.

Aseptic loosening of the prosthesis is another complication in which the use of prosthesis with a rotating hinge has reduced the incidence. Recent reports of using uncemented prosthesis have also reported a reduction in the rates of aseptic loosening.

So these technical modifications have reduced the complication rates in this anatomical site which traditionally has a higher complication rate.

Quality of life assessment

QOL was analysed by the Cancer Institute QOL Questionnaire[31] which is based on 42 questions and based on that scores are given. Higher the scores better the QOL.

The score of the patients undergoing myoplasty was 148.89 which is just above the average score, and the score of the patient undergoing mesh-myoplasty was 144.17 which is in the higher range of average scores. There was no statistically significant difference in the quality of life of the patients undergoing myoplasty or mesh-myoplasty.

None of the factors subgrouped to denote different aspects of the quality of life showed any difference in the two groups except the aspect of information support.

Over all the quality of life was satisfactory.

Functional outcome assessment.

Functional outcome was assessed using MSTS scoring system[30]. The mean MSTS score was 22.35 (74.5%). It was 22.33 in the patients undergoing myoplasty and 22.38 in the

patients undergoing mesh-myoplasty. Comparison of the functional outcome between the two groups was not statistically significant. However while analysing the scores concerned with 'emotional acceptance' there was a statistically significant difference in favour of the group in which the reconstruction was done using mesh-myoplasty.

The MSTS score of our series was comparable with those in the other series.

Study	MSTS score
R. J. Grimer, et al.[9]	77%
Vijay Titus MS[49]	82.1%
Adam J. Schwartz MD et al.[46]	82%
Zhang Y.[50] (tibiofibular joint involved)	70%
Flint MN et al[47]	75%
Our study	74.5%

As compared above the functional outcomes of the patients in our series is satisfactory.

Extensor lag

The active extensor lag for the patients undergoing myoplasty was $68.13^0$and for the patients undergoing mesh-myoplasty was 38.81^0. The difference in the outcomes was statistically significant in favour of the group undergoing mesh-myoplasty (p=0.004). No revision surgeries were done in our surgeries for the repair of the extensor mechanism. The following table compares the outcomes of the extensor lag of our series with that of other series.

Study	Mean Extensor Lag
Our study (myoplasty)	68.13^0
Our study (mesh-myoplasty)	38.81^0
R. J. Grimer, et al.[9]	30^0
Adam J. Schwartz MD et al.[46]	17.9^0
Flint MN et al[47]	6^0
Vijay Titus MS[49]	4^0
Dominkus M[27]	25^0
Gosheger G[26]	7.5^0
Shimose S[51]	26^0

Though the extensor lag in the mesh-myoplasty arm in our series was significantly better than the arm which underwent myoplasty alone, it was more than some of the other studies. The extensor lag in our series could be further improved by

1. Considering revision surgery for the extensor mechanism for patients with poor extension.

2. Extensor mechanism could be augmented with bone grafts, wire cerclage, etc.

CONCLUSION

1. With the use of effective modern chemotherapy osteosarcoma treatment has seen a paradigm shift. Excellent survival results are seen in the proximal tibial osteosarcomas in our study which is at par with the international studies. Patients receiving 3 to 4 cycles of preoperative chemotherapy showed better survival outcome than those receiving 5 to 6 cycles of preoperative chemotherapy, thought it was not statistically significant. Good responders to preoperative chemotherapy also showed a trend towards better survival though it was not statistically significant.

2. Limb salvage surgery has been very satisfactorily done for the proximal tibial osteosarcomas, which is traditionally considered a difficult site to reconstruct.

3. Prosthesis survival at this site is influenced by a high rate of complications which include infection, prosthesis loosening and fracture of the prosthesis. The modifications of the surgical techniques and use of flaps for soft tissue cover has significantly reduced these complications.

4. There was no statistically significant difference in the prosthesis survival times of the patients undergoing myoplasty versus those undergoing mesh-myoplasty.

5. The extensor lag was significantly better in the patients undergoing mesh-myoplasty, but compared to international studies it was slightly inferior. We may need to consider the use of bone grafts augmentation for better bio-integration of the extensor mechanism.

BIBLIOGRAPHY

1. Peltier LF. Tumors of bone and soft tissues. *Orthopedics: A History and Iconography*. San Francisco, Calif: Norman Publishing; 1993:264-91

2. Mallon WJ. The registry of bone sarcoma. *Ernest Amory Codman: The End Result of a Life in Medicine*. Philadelphia, Pa: WB Saunders Co; 2000:107-21.

3. Link MP, Goorin AM, Miser AW, et al. The effect of adjuvant chemotherapy on relapse-free survival in patients with osteosarcoma of the extremity. *N Engl J Med*. Jun 19 1986;314(25):1600-6.

4. Rosen G, Murphy ML, Huvos AG, Gutierrez M, Marcove RC. Chemotherapy, en bloc resection, and prosthetic bone replacement in the treatment of osteogenic sarcoma. *Cancer*. Jan 1976;37(1):1-11.

5. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma.*ClinOrthopRelat Res*. Nov-Dec 1980;153:106-20.

6. Custom made megaprosthesis and limb salvage surgery by Prof Dr MV Natarajan.scripts.tnmgrmu.ac.in/vc/custommegaprosthesis.pdf

7. Huvos AG.*Bone tumors: diagnosis, treatment and prognosis.* Philadelphia,etc: WB Saunders Co, 1979.

8. Schajowicz F. *Tumors and tumorlike lesions of bone: pathology,radiology and treatment.* 2nd ed. Berlin, Springer-Verlag, 1994.

9. R. J. Grimer, et al. J Bone Joint Surg [Br] 1999;81-B:488-94.

10. Endoprosthetic reconstruction in LSS. www.sarcoma.org/publications/mcs/ch25.pdf

11. Picci P, Bacci G, Ferrari S et al. Local recurrence after limb salvage procedures for osteosarcoma: Correlation with margins and chemotherapy induced necrosis. J Bone Joint Surg 1993; 75(Suppl II): 211

12. Endoprosthetic reconstruction in LSS. www.sarcoma.org/publications/mcs/ch31.pdf

13. Alman BA, Krajbich JI, Hubbard S. Proximal femoral focal deficiency: results of rotationplasty and Syme amputation. *J Bone Joint Surg Am*. Dec 1995;77(12):1876-82.

14. Borggreve J. Kniegelenksersatzdurch das in der Beinlangsachse um 180 degree gedrehtefussgelenk.*ArchOrthop*. 1930;28:175-178.

15. Van Nes CP. Rotation-plasty for congenital defects of the femur.Making use of the shortened limb to control the knee joint of a prosthesis. *J Bone Joint Surg*. 1950;32B:12-16.

16. Fowler E, Zernicke R, Setoguchi Y, Oppenheim W. Energy expenditure during walking by children who have proximal femoral focal deficiency. *J Bone Joint Surg Am*. Dec 1996;78(12):1857-62.

17. Malawer MM, Price WM: Gastrocnemius transposition flap in conjunction with limb-sparing surgery for primary bone sarcomas around the knee. PlastReconstrSurg 73:741, 1984

18. Tae Won B. Kim, Richard D. Lackman: Survivorship of Endoprostheses in Bone Tumor Reconstruction. University of Pennsylvania Orthopedic journal.Vol 21, May 2011, pg 69-72.

19. P. S. Unwin, S. R. Cannon, R. J. Grimer, H. B. S. Kemp, R. S. Sneath, P. S. Walker. Aseptic loosening in cemented custom made prosthesis for bone tumours of the lower limbs. J Bone Joint Surg [Br] 1996;78-B:5-13.

20**.** G. J. C. Myers, A. T. Abudu, R. Carter, R. M. Tillman, and R. J. Grimer.The long-term results of endoprosthetic replacement of the proximal tibia for bone tumours.Journal of Bone and Joint Surgery - British Volume, Vol 89-B, Issue 12, 1632-1637.

21. Hejna MJ, Gitelis S. Allograft prosthetic composite reconstruction for bone tumors. SemSurgOncol. 1997;13: 18–24.

22. Edmund W. Ek, Warren M. Rozen, Eugene T. Ek, Hannes A. Rudiger. Surgical options for reconstruction of the extensor mechanism of the knee after limb-sparing sarcoma surgery. Arch Orthop Trauma Surg (2011) 131:487–495

23 Horowitz SM, Lane JM, Otis JC, Healey JH (1991) Prosthetic arthroplasty of the knee after resection of a sarcoma of the proximal end of the tibia: a report of sixteen cases. J Bone Joint Surg 73A:286–293

24 Boris Michael Holzapfel, Hans Rechl, Stefan Lehner, HakanPilge, Hans Gollwitzer,and Erwin Steinhauser. Alloplastic Reconstruction of the Extensor Mechanism after Resection of Tibial Sarcoma.Sarcoma Volume 2011, Article ID 545104, 8 pages.

25. Jacob Bickels, MD, James C. Wittig, MD, Yehuda Kollender, MD,Robert S. Neff, BA, Kristen Kellar-Graney, BA, Isaac Meller, MD,and Martin M. Malawer, MD. Reconstruction of the Extensor Mechanism AfterProximal Tibia Endoprosthetic Replacement. The Journal of Arthroplasty Vol. 16 No. 7 2001.

26. Gosheger G, Hillmann A, Lindner N, Rödl R, HoVmann C, Bürger H, Winkelmann W (2001) Soft tissue reconstruction of megaprostheses using a trevira tube. ClinOrthopRelat Res 393(1):264–271

27. Dominkus M, Sabeti M, Toma C, Abdolvahab F, Trieb K, Kotz RI (2006) Reconstructing the extensor apparatus with a new polyester ligament. ClinOrthopRelat Res 453(1):328–334

28. Malawer MM, Price WM (1984) Gastrocnemius transposition flap in conjunction with limb-sparing surgery for primary bone sarcomas around the knee. PlastReconstrSurg 73:741–750

29. Edge SB, Byrd DR, Compton CC, et al. AJCC cancer staging manual, 7th ed. Newyork: Springer, 2010.

30. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumours of the musculoskeletal system.ClinOrthop 1993;286:241-6.

31. E Vidhubala, Latha, R Ravikannan, CS Mani, R Muthuvel, V Surendren, FU John Paul**.** Validation of Cancer Institute Quality of Life Questionnaire Version II for cancer patients in India. Indian Journal of Cancer Vol:48, Issue:4, Page 500-506

32. Stefan S. Bielacket. al, Prognostic Factors in High-Grade Osteosarcoma of theExtremities or Trunk: An Analysis of 1,702 PatientsTreated on Neoadjuvant Cooperative Osteosarcoma StudyGroup Protocols. Journal of Clinical Oncology, Vol 20, No 3 (February 1), 2002: pp 776-790.

33. Bacci G, Ferrari S, Bertoni F, Ruggieri P, Picci P, LonghliA et al. Long term outcome for patients with nonmetastatic osteosarcoma of the extremity treated at the InstitutoOrthopedico Rizzoli according to the InstitutoOrthopedico Rizzoli/ Osteosarcoma -2 protocal: an updated report. J ClinOncol 2000; 18:4016-27

34. A. SérgioPetrilli et al. Results of the Brazilian Osteosarcoma Treatment Group Studies III and IV: Prognostic Factors and Impact on Survival. J ClinOncoVol 24; Number 7. March 2006.

35. Spanier SS, Shuster JJ, Vander Griend RA. The effect of local extent of the tumor on prognosis in osteosarcoma.J Bone Joint Surg Am. 1990 Jun;72(5):643-53.

36. Allen M. Goorin et al. Presurgical Chemotherapy Compared With Immediate Surgery

andAdjuvant Chemotherapy for NonmetastaticOsteosarcoma:Pediatric Oncology Group Study POG-8651. Journal of Clinical Oncology, Vol 21, No 8 (April 15), 2003: pp 1574-1580

37. Huvos AG, Rosen G, Marcove RC. Primary osteogenic sarcoma: pathologic aspects in 20 patients after treatment with chemotherapy en bloc resection, and prosthetic bone eplacement. Arch Pathol Lab Med 1977;101(1):14.

38. Salzer-Kuntschik M, Delling G, Beron G, et al. Morphological grades of regression in osteosarcoma after polychemotherapyâ€”study COSS 80. J Cancer Res ClinOncol 1983; 106(Suppl):21.

39. Picci P, Bacci G, Campanacci M, et al. Histologic evaluation of necrosis in osteosarcoma induced by chemotherapy. Regional mapping of viable and nonviable tumor.Cancer 1985;56(7):1515.

40. SigbjornSmeland et al. Scandinavian experience in classical osteosarcoma, results of the SSG XIV protocol. ActaOrthopaedica (Suppl 334) 2009;80.

41. P. Picci et al. Risk factors for local recurrences after limb-salvage surgery for high-grade osteosarcoma of the extremities. Annals of Oncology 8: 899-903, 1997.

42. D. Andreouet al. The influence of tumor- and treatment-related factors on the development of local recurrence in osteosarcoma after adequate surgery. An analysis of 1355 patients treated on neoadjuvant Cooperative Osteosarcoma Study Group protocols. Annals of OncologyVolume22, Issue5Pp. 1228-1235.

43. Torbert, Jesse T MD et al. Endoprosthetic Reconstructions: Results of Long-term Followup of 139 Patients. Clinical Orthopaedics & Related Research: September 2005 - Volume 438 - Issue - pp 51-59

44. Bacci G et al. Predictive factors for local recurrence inosteosarcoma. ActaOrthopScand 1998; 69 (3): 230-236

45. MayilVahananNatarajan, A. Sivaseelam, G. Rajkumar and S. H. JaheerHussain. Custom megaprosthetic replacement for proximal tibial tumours.International Orthopedics, Volume 27, Number 6, 334-337

46. Adam J. Schwartz MD, J. Michael Kabo PhD,Fritz C. Eilber MD, Frederick R. Eilber MD,Jeffrey J. Eckardt MD. Cemented Endoprosthetic Reconstruction of the Proximal Tibia.ClinOrthopRelat Res (2010) 468:2875–2884.

47. Flint MN, Griffin AM, Bell RS, Ferguson PC, Wunder JS.Aseptic loosening is uncommon with uncemented proximal tibiatumor prostheses. ClinOrthopRelat Res. 2006;450:52–59

48. Wu CC, Henshaw RM, Pritsch T, Squires MH, Malawer MM.Implant design and resection length affect cemented endoprosthesissurvival in proximal tibial reconstruction. J Arthroplasty.2008;23:886–893

49. Vijay Titus MS (Orth), Dip Orth, Mark Clayer MD, MBBS, FRACS, FAOrthA. Protecting a Patellar Ligament Reconstruction after ProximalTibial Resection.ClinOrthopRelat Res (2008) 466:1749–1754

50. Zhang Y, Yang Z, Li X, Chen Y, Zhang S, Du M, Li J**.** Custom prosthetic reconstruction for proximal tibial osteosarcoma with proximal tibiofibular joint involved. SurgOncol. 2008 Aug;17(2):87-95

51. Shimose S, Sugita T, Kubo T, Matsuo T, Ochi M. Reconstructed patellar tendon length after proximal tibia prosthetic replacement. ClinOrthopRelat Res. 2005;439:176–180

ABSTRACT

Limb salvage surgery in osteosarcomas of the upper end of the tibia encompasses several challenges. Among those challenges lack of soft tissue cover, higher rates of prosthesis failure and difficulty in reconstructing extensor mechanism of the knee joint are important.

Retrospective analysis of 41 consecutive patients undergoing limb salvage surgery for proximal tibialosteosarcomas at our institute from 2001 to 2011.16 patients underwent reconstruction with endoprosthesis and myoplasty (gastrocnemius muscle flap) and 25 patients underwent reconstruction with mesh-myoplasty (using prolene mesh for reconstruction of the extensor mechanism). The 5 yr overall survival and disease free survival was 85.5% and 70.6%. Patients who has 3 to 4 cycles of preoperative chemotherapy had significantly better 5 year overall survival then those who received 5 to 6 cycles of chemotherapy. (94.1% versus 68.6%). 9 patients (22%) had tumour necrosis >90% and 32 patients (78%) had tumour necrosis =<90%, but there was no statistically significant difference in the overall survivals of these two groups (87.5% versus 84.6%). The mean prosthesis survival was 34.5 months (range 2.3 months to 133.1 months). The 5 year prosthesis survival was 86.5%. Infection (3), aseptic loosening (3) and fracture of the prosthesis (2) were the main reasons for prosthesis failure. There was no statistically significant difference in the prosthesis survival between the cases that underwent myoplasty and meshmyoplasty.

Quality of life analysis was done using the Cancer Institute QOL questionnaire II and functional outcomes were evaluated with MSTS scoring system (mean score 74.5%). There was no statistically significant difference in the quality of life outcomes or functional outcomes according to these scoring systems. But the mean extensor lag in the patients undergoing myoplasty was 68.13^0 and the mean extensor lag in the patients undergoing mesh-myoplasty was 36.66^0 and the difference was statistically significant (p=0.004). 2 patients with meshmyoplasty had 0^0 extensor lag whereas none of the patients with myoplasty had 0^0 extensor lag.

8 patients had lung metastasis, 1 patient had local recurrence and 1 patient had both local recurrence and lung metastasis.

The prosthesis survival and the functional outcomes (MSTS scores) in our series is comparable to the other series in literature on endoprosthetic reconstruction for proximal tibial osteosarcomas.

Keywords: Custom made endoprosthesis, proximal tibial osteosarcoma, limb salvage surgery